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ASTHMA IN CHILDREN

I. ETIOLOGY *

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The present-day conception of the exciting factors which cause asthma differs considerably from that of former years. Toward this newer conception a voluminous literature has been contributed, beginning with the pioneer studies of Schloss, Walker, Koessel, Cooke and others; yet, with all this vast accumulation of valuable material, the number of communications devoted only to asthma in children is strikingly small. These deal mainly with special phases of asthma and are of a statistical character most often lacking in essential details; in those communications reporting a large number of cases, the observations covered too short a period of time to permit satisfactory conclusions.

The material for this and for subsequent studies is based on 100 consecutive cases of asthma, 92 per cent of which are Jewish children, living on the East Side of Harlem, and ranging in age from 6 months to 14 years. All of these subjects were under observation from one to four years, the average being two and one-third years.

Asthma is a clinical syndrome, quite readily diagnosed on physical examination of the patient. The diagnosis once made, all investigators of this disease proceed to search for the etiologic or exciting factors responsible for the presenting symptoms. Some authors would restrict the term asthma only to those patients exhibiting protein hypersensitiveness (anaphylaxis, allergy, atopy). Such a point of view is erroneous, since asthma is nothing more than a recurring dyspnea, more marked in expiration associated with wheezing, and the exciting cause may or may not be protein sensitization.

To depend on the elicitation of protein sensitization alone would lead one astray. Therefore, the procedure to employ in a search for the etiologic basis of asthma involves, in addition to the cutaneous protein tests, a carefully taken detailed history and a thorough physical examination, employing roentgen rays, the Pirquet test, laboratory and other diagnostic aids.

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* From the Children's Asthma Clinic, Mt. Sinai Hospital.

The importance of securing a proper history cannot be overemphasized. The history has a direct and significant bearing on the interpretation of the protein skin tests and other clinical findings. It often dictates the form of therapy to be instituted. The following history form, while far from being perfect, has served to cover in a practical manner almost every possible question pertinent to this subject. The average time required to take such a history in experienced hands was one-half hour.

HISTORY

(When recording any data, state the age of the patient with the month and year of the event.)

A. Past History:

1. *Infancy.*—Breast fed? First bottle, and how prepared? When were other foods given and what were the disturbances, if any? Is there a history of "recurrent bronchitis," "rhinitis" or vomiting? If so, can these conditions be associated with foods and other proteins? Were there eczema or other skin diseases? If so, age of onset, period of duration and parts affected?

2. *Onset of Asthma.*—Age? Month or season of the year? Gradual or sudden? Was there a history of wheezing, repeated attacks of bronchitis, catarrhal symptoms of the nose and conjunctiva prior to the onset of bronchospasms? If so, describe in detail. What association, if any, was there between the age of onset of the bronchospasms, attacks of wheezing or "recurrent bronchitis" to other diseases, such as pneumonia, pertussis, scarlet fever; to operations, tonsillectomy and adenoidectomy, and to serum injections, diphtheria or other antitoxins? Describe in detail. If eczema, urticaria or angioneurotic edema occurred prior to or after the onset of asthma, state the interval of time between these conditions and its relation to the asthmatic state.

3. *Course of Asthma.*—Trace the asthmatic state from its inception to the present time with reference to the frequency and duration of the attacks. Describe any special features that may have been associated with the attacks, such as fever, vomiting or "nose colds." Was there a definite history of freedom from asthmatic symptoms between attacks? If so, what are the longest and shortest intervals? What was the patient's mode of living, his condition of physical health? Was he free from intercurrent infections during these intervals of freedom from asthma? If wheezing was present between attacks, describe in detail.

4. *Environmental Contact and Exposure.*—What is the clinical effect of foods, dust, domestic animals, hair or feather pillows, mattresses, fur coats, fur trimmings (collars or cuffs), blankets, furniture stuffing or toys? What is the effect of sudden changes in weather and seasons; present and past environments; and changes in climate, when, where and duration of stay? What is the occupation of all the members of the household? Are there any stables, poultry markets, butcher shops or garages around the present home? What was the effect of intercurrent infections or other diseases, such as upper respiratory infections, grip, pneumonia, acute exanthemas, etc., on the asthmatic state? What was the effect of tonsillectomy or other operation and injection of antitoxin or serums on asthma?

5. *Other Diseases.*—What other diseases did the child have that were not mentioned in the preceding history, and what was the effect on the asthmatic state?

B. Family History:

Was there a history of early or late hay-fever, asthma, eczema, urticaria or angioneurotic edema in the father, mother, brothers, sisters or maternal and

paternal grandfathers, grandmothers, aunts and uncles? Was there tuberculosis, syphilis or rheumatism in the parents?

C. Present Symptoms and Diet:

Cough, productive or not, nasal discharge, dyspnea, sleep, appetite, bowels, pain, headache, diet.

D. Summary and Comment.

A thorough physical examination is essential. Search for structural changes, endocrine dysfunction, gastro-intestinal disturbances and for foci of infection should be carefully made. The state of nutrition of the child should be noted. Roentgenoscopy of the chest, Pirquet and intradermal tuberculin tests and urinalysis are routinely performed.

CLASSIFICATION OF ASTHMA

From the history it is possible to group all cases of asthma into the first important subdivision with relation to the onset, as follows:

1. Acute Onset: This type of asthma occurs in definite paroxysms, which may last from a few hours to several days; during the interval between attacks, the patient is completely free from all asthmatic signs and symptoms. Or, asthma may be continuous from the onset, with varying periods of remission. Asthma occurring within several weeks of an infective illness is also included in this group. Thirty-nine per cent of the cases of this series were of acute onset.

2. Insidious Onset: This type of asthma is characterized by the appearance of wheezing and dyspnea after repeated attacks of "bronchitis," "rhinitis" or the so-called "noninfective cold." These may or may not have direct relation to the seasons of the year. The symptoms, in this early stage, are not so severe as those observed in the type with acute onset, and are frequently wrongly diagnosed as acute or subacute bronchitis. These mild attacks are of definite duration, and during the intervals of remission there may be a cough and some wheezing or complete freedom from symptoms. Later, typical asthmatic attacks develop. The attacks are often preceded by a definite upper respiratory infection. In subjects more severely ill, chronic bronchitis usually develops, associated with continuous wheezing and exacerbation of asthmatic attacks of varying severity. This type is often referred to as "asthmatic bronchitis," which is misleading since it implies, according to many authors, an absence of protein sensitization, and many of these children belong to the true protein sensitive group. Sixty-one per cent of this series come under this group.

ETIOLOGIC CLASSIFICATION

With the introduction of the protein skin tests, a practical method of classification of asthma along etiologic lines was possible for the first time. These protein skin tests, supported by physical and laboratory

findings, afford a new classification of extreme value since it leads directly to rational therapy. In this classification there are three main groups which are inclusive of all types of asthma.

A. Protein sensitive asthma.
B. Nonprotein sensitive asthma.
C. Para-asthma, a new term which will be dealt with under the proper heading.

Of the 100 cases, 79 per cent were classified as protein sensitive; 18 per cent as nonprotein sensitive, and 3 per cent as para-asthma.

(A) PROTEIN SENSITIVE ASTHMA

The substances that are known to be etiologic factors in asthma are classified into the following groups.

1. Inhalants:
   - Epidermal proteins.
   - Dust.
   - Orris root and sachets.
   - Insecticides.
2. Food.
3. Pollen.
4. Bacteria.
5. Therapeutic animal serums.
6. Drugs.

The paths of absorption of the proteins may be the respiratory, gastro-intestinal and parenteral routes, or by absorption from a focus.

Proteins Used in Skin Testing.—Taking into consideration the diet and environment of the majority of the children tested, the following ninety-seven proteins were, therefore, routinely employed.

Wheat (whole)
Wheat gliadin
Wheat glutenin
Wheat globulin
Wheat proteose
Wheat leucosin
Barley
Buckwheat
Corn
Oat
Rice
Rye

Egg-whole
Egg-white
Egg-yolk
Milk (cow's)
Casein
Lactalbumin
Cheese

Cocoa

Almond
Brazil nut
Chestnut
Peanut
Walnut

Asparagus
Beet
Bean
Cabbage
Carrot
Cucumber
Lentil
Lettuce
Lima bean
Mustard
Onion
Pea
Potato

Salmon
Smelts

Banana
Fig
Orange
Pear
Pineapple
Strawberry

Ragweed, short
Ragweed, tall
Goldenrod
Goldenglow
Sunflower
Corn
Daisy
Timothy
Red-top
Orchard grass
June grass

Streptococcus hemolyticus
Streptococcus nonhemolyticus
Pneumococcus Type 1
Pneumococcus Type 2
Pneumococcus Type 3
Bacillus coli
Friedländer Bacillus
Pertussis Bacillus

House dust
Rabbit hair
Horse dander
Horse serum
Duck feathers
Goose feathers
Chicken feathers

Beef	Radish	*Staphylococcus pyogenes-aureus*	Cat hair
Chicken	Rhubarb	*Staphylococcus pyogenes-albus*	Dog hair
Goose	Spinach	*Staphylococcus pyogenes-citreus*	Goat hair
Lamb	Tomato	*Streptococcus viridans*	Cattle hair
Veal			Camel hair
	Herring		Sheep wool
Coffee	Mackerel		Orris root
Tea	Pike		

Since this series of cases was commenced in 1922, protein substances, such as pyrethrum, glue, kapoc, silk floss and others, have come into use for routine testing, and therefore are not found in the preceding list of proteins.

SELECTION OF PROTEIN

It is important to select the proper proteins for the skin tests, since these substances are one of the most essential working tools which the physician has at his disposal to reveal the etiologic factor in asthma, as well as to enable him to differentiate those who are protein sensitive from those who are nonprotein sensitive.

The proper selection of proteins by the vast majority of practitioners who are compelled to depend on an outside source of supply has been made more and more difficult. In the past few years, many pharmaceutical houses have marketed these protein substances. Each concern prepares them differently, and some sacrifice potency for convenience of preparation. The proteins employed in this series were in powder form and were prepared under the methods and supervision of R. P. Wodehouse. Before being used, the activity of the proteins, so far as possible, was tested on subjects known to be positively sensitive, and was also checked with proteins prepared by me. In this manner it was possible at all times to employ proteins possessing a high standard of potency.[1]

A physician owes it to his patient and to himself to become familiarized with the potency of the proteins employed as a diagnostic aid in the search for an etiologic factor. To disregard this admonition only invites increasing confusion and failure in the treatment of the distressing asthma symptoms.

TECHNIC OF THE TESTS

As a routine, the cutaneous scratch test was employed. The technic of the tests and the discussion of skin irritability has been previously described in detail.[2] The immediate reactions were read within thirty minutes from the application of the protein.

1. It is not within the scope of this paper to enter into a discussion concerning the chemical extraction and precipitation of various proteins, but I am convinced from personal experience that many proteins can be made in powder form which will maintain a high degree of potency for at least three years and perhaps for many more.

2. Peshkin, M. M., and Rost, W. L.: The Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child. **23**:51 (Jan.) 1922.

At times, it was found necessary to resort to the conjunctival or ophthalmic test in patients in whom a positive or suspicious history of sensitization to pollens was elicited with negative scratch tests. During the pollenating season, the pollen causes symptoms by direct contact with the mucous membranes of the susceptible person. In those in whom the skin proved to be insensitive, natural, properly prepared pollen, placed directly on the mucous membrane of the lower lid, will produce a positive reaction within one to five minutes, depending on the degree of sensitivity. This reaction can be removed in a few minutes with several drops of a solution of epinephrine hydrochloride (1 : 1,000). The occurrence of nonspecific irritation has not been noticed in a large series of normal controls. The main purpose of this test is to determine, not the degree of sensitivity, but, rather, the absence or presence of sensitization when skin sensitization is absent.

TYPES OF REACTION

In an effort to create uniformity in recording the protein skin reactions, the following schema was adopted and found satisfactory and practical. In order to avoid the usual method of designating reactions as plus-minus, doubtful and one, two, three or four plus, the vowels, A, E, I, O and U were employed. Pirquet [3] in his studies on nutrition first employed the vowels to designate the condition of the stools, vomiting, etc. However, in order to avoid confusion, the reactions recorded in this paper will be designated by the usual system.

(A) POSITIVE REACTIONS

1. One plus is an 0 reaction. This is a distinct urticarial wheal, 0.5 cm. in diameter, surrounded by a zone of erythema in the presence of a negative control; or a distinct urticarial wheal less than 0.5 cm. in diameter, surrounded by a zone of erythema of two or more centimeters; or only a zone of erythema of two or more centimeters with little or no elevation around the cut.

2. Two plus is an A reaction, which is an urticarial wheal from 0.6 cm. to 0.7 cm. in diameter, with or without a surrounding zone of erythema.

3. Three plus is an E reaction, which is an urticarial wheal from 0.8 cm. to 0.9 cm. in diameter, with or without a surrounding zone of erythema.

4. Four plus is an I reaction, the urticarial wheal measuring one centimeter or more in diameter with or without a surrounding zone of erythema.

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3. Pirquet, Clemens: System der Ernahrung, Berlin, Julius Springer, 1917.

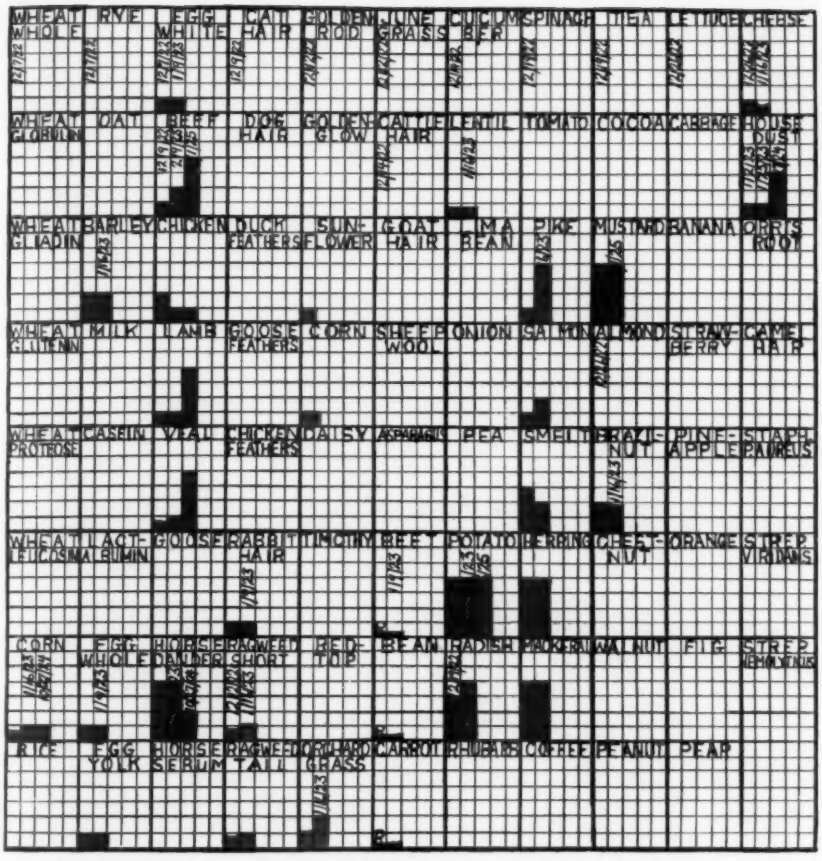

Chart 1.—The recording of the skin tests. The various protein groups are designated by color. Red denotes food proteins. Blue denotes all inhalant proteins except pollen which is green. All proteins, including bacteria, not covered in the preceding groups are colored blue.

The skin reactions are read from the base line up, as follows: the base line corresponds to a negative reaction, half a square is a plus-minus reaction, one square a one plus, two squares a two plus, three squares a three plus and four squares a four plus reaction. The name of the protein is printed above the reaction and the date of the test is recorded between. Every reaction above the control is repeated on a different day than when the test was performed, and for this purpose sufficient parallel columns were allotted so that a record of the comparative reactions can be observed at a glance. R — repeat.

5. All reactions measuring less than the foregoing and more than the control, formerly designated as a doubtful or plus-minus reaction but is a positive reaction, as will be shown, is now an OU reaction.

(B) DELAYED REACTIONS

This reaction is described by Walker as negative at the end of one-half hour, but on the following day the cut appears similar to a slight infection; the surrounding skin is hot, very red and elevated. Frequently the cut contains pus which is always sterile. This reaction was not often observed to occur in this series because the patients were not seen for the twenty-four hours following the tests. Delayed reactions are recorded in the same manner as the immediate reactions; in the former instance the size of the induration replaces the wheal occurring in the latter.

(C) NEGATIVE REACTION

This reaction is designated as an U reaction, which does not differ in any way from the control.

METHOD OF RECORDING THE SKIN TESTS

When the protein skin tests were completed, it was found that much valuable time and effort was wasted in making a summary of reactions as it is usually recorded. The recording of the skin tests, as shown in chart 1, proved to be an easy and time saving method which was permanently adopted.

GENERAL REACTIONS FOLLOWING CUTANEOUS TESTS

Immediate or delayed general (constitutional) reactions following cutaneous tests have not been observed to occur in this series, nor has it ever occurred in my experience. From a review of the literature, such reactions are exceedingly rare and never fatal. However, it has been mentioned by Brown [4] and Cooke,[5] who cite the same case of a general reaction produced by Rufus Cole with buckwheat after a scratch test reported by H. L. Smith in 1909. Some years ago, Cooke [5] also witnessed a case of general reaction from a scratch test to timothy.

The rarity of occurrence of a general reaction following a scratch test, properly performed, does not depend on the potency of the protein, but rather the edema accompanying a positive reaction seals the cut and prevents further absorption of the protein. By virtue of it being a scratch test, there is the slowest possible absorption of protein and the

4. Brown, Aaron: Studies in Specific Hypersensitiveness. I. The Diagnostic Cutaneous Reaction in Allergy. Comparison of the Intradermal Method (Cooke) and the Scratch Method (Schloss), J. Immunol. **7**:97 (March) 1922.

5. Cooke, R. A.: Studies in Specific Hypersensitiveness. III. On Constitutional Reactions. The Dangers of the Diagnostic Cutaneous Test and Therapeutic Injection of Allergens, J. Immunol. **7**:119 (March) 1922.

reaction thereby becomes purely local in its effect. It has been previously stated that when a series of skin tests were completed, all the positive reactions were repeated for confirmation. As a result of this procedure, as many as ten or more positive reactions have been elicited at one sitting without the slightest evidences of an immediate or delayed general reaction.

RELATION OF PROTEIN SKIN REACTIONS TO THE ETIOLOGY OF ASTHMA

In order to clarify our ideas regarding the etiology of asthma, it becomes essential to lay down certain basic requirements, at least one of which must be fulfilled before we can assume that any protein is etiologically important in a given case of bronchial asthma.

1. Sensitization must be demonstrated by a conjunctival or a local cutaneous reaction.

2. The association of the patient's contact with the suspected protein and the production of clinical symptoms should be demonstrated if possible.

3. The symptoms must be relieved or greatly improved on withdrawal of, or by treatment with, the suspected protein.

I do not deem it wise nor always safe to subject a sensitive individual to a subcutaneous injection of the offending protein in order to demonstrate cause and effect. This experiment is not without possible serious or even dangerous consequences. Several deaths have been reported, and deaths are known to have occurred that were not reported.

It is well known that every sensitive patient has acquired a certain degree of protein tolerance. The findings of a cutaneous reaction does not necessarily predicate symptoms. Some sensitizations have been previous etiologic factors, but play no rôle in the existing cause of asthma. Then again, sensitization may be present and symptoms may be due to other factors. Bearing these points in mind, it is important, therefore, to differentiate between etiologic and nonetiologic protein sensitization.

Etiologic protein sensitizations can be determined with ease in some patients. Some require further study and perhaps treatment before an etiologic sensitization can be found. In another group, the etiologic proteins are extremely difficult or almost impossible to determine with any degree of certainty, and in other cases the multiplicity of sensitizations present played no part in the existing etiology of asthma.

The size of the cutaneous reaction to a substance does not determine its importance in the etiology. The size of the reaction depends on the concentration of the offending substance in the test material used. In the preparation of the test material, the concentration of the etiologic

substance may be small and therefore the reaction procured may be comparatively insignificant. Furthermore, the size of the reaction with the same test material on the same person at different times varies greatly. In a recent publication, Piness and his co-workers [6] published some pertinent facts concerning the varying activity of protein preparations made with various extractives, which lend support to these statements. It is important then that small reactions should not be ignored. It has been my repeated experience to observe patients presenting one to four plus and plus minus reactions who have been improved or entirely relieved of their symptoms, when one or all of the latter were seriously considered as etiologic factors.

In this series of 100 children, interpreting all reactions above the control as significant, 79 per cent were considered protein sensitive. According to the Walker classification, 75 per cent would have been considered as subjects with allergic asthma.

Walker [7] reports 136 patients with asthma, with onset from infancy to 15 years, 69 per cent of whom were considered protein sensitive. Since only the age of onset of asthma was considered, many of these patients probably were adults when tested. This differentiation involves a point which will be shown later to have considerable bearing on the final interpretation.

Herman [8] reports thirty-one cases of asthma in children (New York City), with onset from 6 months to 10 years of age, of varied nationalities, including negroes, of whom 55 per cent were protein sensitive. An average of ninety-six different proteins were tried in each case. Important inhalant substances such as house dust, orris root, duck feathers and goat hair were not employed. Ten reactions (including all reactions above the control) were the average number per patient.

Larsen and Bell,[9] in a study of 100 children (New York City), found only 44 per cent protein sensitive. This low figure does not account for the actual number of hypersensitive children they encountered, as only those reactions in which the wheal measured 1 cm. or more, were considered. The basis for such a classification is difficult to understand and appears to be empiric. The number of cases recorded

6. Piness, G.; Miller, H., and Alles, G. A.: Comparative Methods of Protein Extraction with Chemical and Clinical Studies, J. A. M. A. **83**:608 (Aug. 23) 1924.

7. Walker, I. C.: Clinical Study of 400 Patients with Bronchial Asthma, Boston M. & S. J. **179**:288 (Aug. 29) 1918.

8. Herman, Harold: A Critical Study of Sixty-one Cases of Asthma and Eczema in Infancy and Childhood Controlled by Cutaneous Protein Sensitization Tests, Am. J. Dis. Child. **24**:221 (Sept.) 1922.

9. Larsen, N. P., and Bell, S. D.: Classification and Management of Asthma in Childhood. The Importance of Rabbit Hair as a Cause in New York City, Am. J. Dis. Child. **24**:441 (Nov.) 1922.

as nonprotein sensitive but showing cutaneous reactions were not stated. The number of tests tried on each patient varied from seven to forty-five.

The data published are so confusing that, in order to derive any conclusions of value, it is essential that the basic differences of the data from which the results are deduced should be studied comparatively as to age, age of onset, age when first observed, environment, nationality, contact, potency and number of proteins employed, method of testing and interpretation of the reaction.

SUMMARY OF CASES

Table 1 is a summary of all the patients exhibiting protein skin reactions above the control.

Fifty-four patients, or 68 per cent, were males and twenty-five patients, or 32 per cent, were females.

TABLE 1.—*Summary of the Protein Sensitive Cases with Relation to the Age of Onset of Asthma*

Age of Onset of Asthma	Number of Patients	Number Positive Reactions			Average Number Reactions per Patient			Actual Number Patients with + Reactions
		+	±	Total	+	±	Total	
1	8	24	15	39	3	2	5	8
2	17	113	71	184	7	4	11	15
3	14	36	59	95	3	4	7	14
4	14	51	61	112	4	4	8	14
5	7	16	17	33	2	2	4	6
6	7	47	34	81	7	5	12	7
7	3	8	8	16	2	3	5	3
8	2	9	10	19	4	4	8	2
9	6	14	12	26	2	2	4	5
10	1	1	2	3	1	2	3	1
Total.....	79	319	289	608	4	3.5	7.5	75

Chart 2 shows the age of onset of asthma of this series, and the age at which they first came under observation. It shows that the onset of asthma is more frequent at 2 years than at any other age, representing 21 per cent of the patients of this group; that the onset of asthma prior to 1 year of age is relatively uncommon; and, as the children approach the age of ten, the allergic incidence seems to become progressively less. No patients developed asthma after the age of 10. This is in accord with the findings of Herman [8] and of Larsen and Bell.[9] The latter observation cannot be viewed as a coincidence; considering that this period is the age of puberty, it seems to have some clinical significance.

It should be noted that the earliest age at which these children first came under observation was 3 years; the majority sought consultation after 5 years of age, the peaks occurring at 7 and 11 years. The period of time elapsing between the onset of asthma and presentation for observation range from a few weeks to 11 years, an average of

4.14 years. The average age of onset was 3.9 years, the earliest case occurred at 6 months and the oldest at 10 years. The series of Larsen and Bell[9] show the age of onset of protein sensitive asthma occurred from birth to 11 years, the average age of onset being 3.7 years and the average duration was 5.92 years.

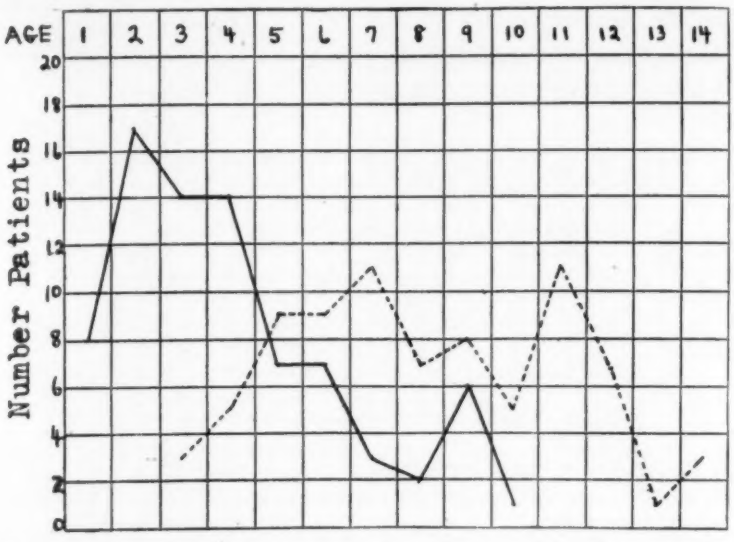

Chart 2.—The number of patients in the protein sensitive group in relation to the age of onset of asthma (plain line), and the age when first seen (broken line).

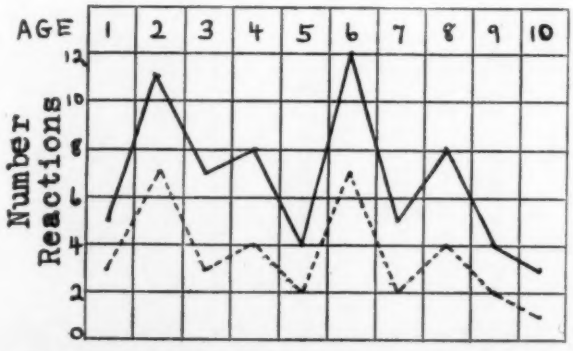

Chart 3.—The average number of positive protein skin reactions per patient in relation to the age of onset of asthma. Plain line, total positive reactions. Broken line, one to four plus reactions only.

Chart 3 shows the average number of reactions per patient in relation to the age of onset. The greatest number of positive skin reactions occurred at the ages of 2 and 6 years, showing 11 and 12 reactions respectively. The largest number of reactions in a single patient was

37; five other patients had from 20 to 30 reactions each; four patients from 15 to 20 reactions; eight patients from 10 to 15 reactions; thirty-three patients from 5 to 10 reactions; twenty-four patients from 2 to 5 reactions; and four patients had only 1 reaction.

It is interesting to note that the curve (chart 3) representing one to four plus reactions shows the same contour as the one representing the total positive reactions.

Table 2 is a summary of the total number of positive reactions in relation to the age when the patients were first tested.

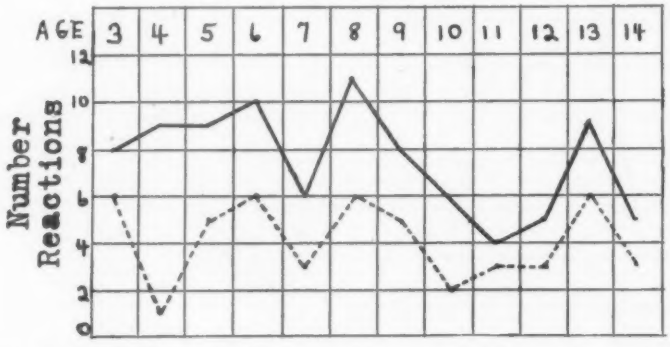

Chart 4.—The average number of positive protein skin reactions per patient in relation to the age when first seen. Plain line, total positive reactions. Broken line, one to four plus reactions only.

TABLE 2.—*Summary of the Protein Sensitive Cases with Relation to the Age When First Tested*

Age First Tested, Years	Number of Patients	Number Positive Reactions			Average Number Reactions per Patient			Actual Number Patients with + Reactions
		+	±	Total	+	±	Total	
3	3	17	6	23	6	2	8	2
4	5	8	38	46	1	8	9	5
5	9	45	37	82	5	4	9	9
6	9	51	42	93	6	5	10	9
7	11	35	32	67	3	3	6	10
8	7	44	36	80	6	5	11	7
9	8	40	26	66	5	3	8	8
10	5	12	19	31	2	4	6	4
11	11	35	24	59	3	2	5	11
12	7	21	17	38	3	2	5	6
13	1	6	3	9	6	3	9	1
14	3	5	9	14	2	3	5	3
Total.....	79	319	280	608	4	3.5	7.5	75

The average number of reactions per patient in relation to the age when the patient was first tested is shown in chart 4. The multiplicity of reactions are greatest between 3 and 10 years, averaging from 6 to 11 reactions per patient with the peak at 8 years. The peak at 13 years should not be considered, since it represents one patient with nine reactions.

INHALANT PROTEINS

Ninety-eight per cent of the allergic patients were sensitive to one or more substances of the inhalant group. This would indicate that any child exhibiting protein sensitization nearly always is sensitive to some inhalant. This observation is somewhat at variance with the earlier views that food sensitization was more commonly met than any other protein group.

There was an average of four inhalant reactions per patient. Chart 5 shows the average number of inhalant reactions per patient in relation to the age of onset.

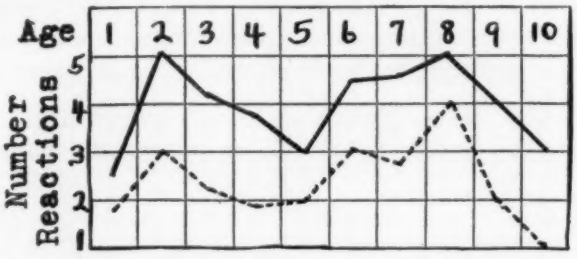

Chart 5.—The average number of positive inhalant skin reactions per patient in relation to the age of onset of asthma. Plain line, total positive reactions. Broken line, one to four plus reactions only.

TABLE 3.—*Size and Incidence of Inhalant Skin Reactions (Not Including Pollen)*

	Rabbit Hair	House Dust	Duck Feathers	Horse Dander	Cat Hair	Goose Feathers	Goat Hair	Dog Hair	Orris Root	Sheep Wool	Camel Hair	Chicken Feathers	Cattle Hair
±	9	16	17	11	14	14	10	10	7	5	8	3	1
+	6	17	11	9	7	1	4	1	4	3	0	3	0
++	10	6	5	5	2	2	2	1	0	1	0	0	1
+++	8	3	3	4	0	0	0	1	1	1	0	0	2
++++	16	4	5	11	1	0	0	0	0	0	0	0	0
Total*	49	46	41	40	24	17	16	13	12	10	8	6	4
Percentage of sensitive group.....	62	58	51	50	30	21	20	16	15	12	10	7	5

* When read as percentages, these figures represent the incidence of the inhalant sensitizations that occurred in the entire series.

Table 3 gives a summary of the inhalants used in this series, indicating the size of the reactions and their incidence in relation to the protein sensitive group and to the entire series of cases.

In their order of frequency, the five most common inhalant sensitizations (excluding pollen) are rabbit hair, house dust, duck feathers, horse dander and cat hair.

Chart 6 shows the average number of inhalant reactions per patient in relation to the age when first coming under observation. It will be noted from this chart that the number of reactions per patient has a fairly even distribution in contradistinction to the peaks at 2 and 8 years, when studied in relation to the age of onset (chart 5). The abnormal peak at 13 years (chart 6) should be disregarded, since it accounts for only one multiple sensitive patient.

Chart 7 represents the most common inhalant sensitizations as they occurred in this series. These charts are conveniently grouped so that the comparative curves may be more easily seen. The peak of reaction in relation to the age of onset occurs mostly at 2 years. With the age of onset after 10 years, there were no reactions to house dust and feathers. With rabbit hair and horse dander, none reacted after 9 years. The number of patients reacting in relation to the age when first tested

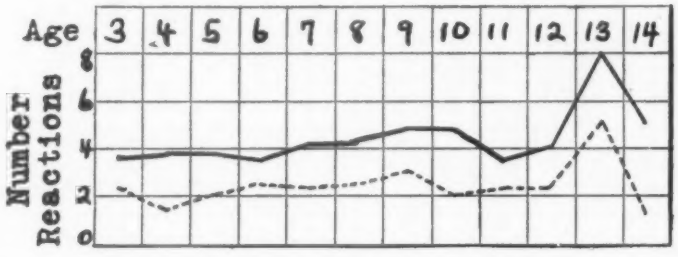

Chart 6.—The average number of positive inhalant skin reactions per patient in relation to the age when first seen. Plain lime, total positive reactions. Broken line, one to four plus reactions only.

show peaks at 7 and 11 years. Duck and goose feathers were combined in one chart because these feathers are so often found mixed in the pillows of this class of children. The combined feather proteins accounted for a total of 58 reactions in forty-four patients.

SENSITIZATION TO RABBIT HAIR

In 1920, Vander Veer [10] cited the first case in the literature in which asthma was caused by rabbit hair found in the pillow on which the patient slept. At that time this author considered this case an unusual occurrence, and little realized its significance nor the widespread prevalence of rabbit hair as a causation of asthma, particularly in the City of New York. In 1922, he [11] reported ninety-three cases, with patients of all ages, showing 9 per cent reacting to rabbit hair.

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10. Vander Veer, A., Jr.: The Asthma Problem, New York M. J. **112**:392 (Sept. 18) 1920.

11. Vander Veer, A., Jr.: The Present Status of the Treatment of Hay-Fever and Asthma, Am. J. M. Sc. **164**:97 (July) 1922.

De Besche [12] reported two cases with positive rabbit hair reactions. The source of exposure, however, was not stated.

Ratner [13] reported eight cases of asthma, the subjects being from 20 months to 9½ years of age, in whom rabbit hair was the sole etiologic factor. The age of onset of asthma ranged from 6 months to 4 years.

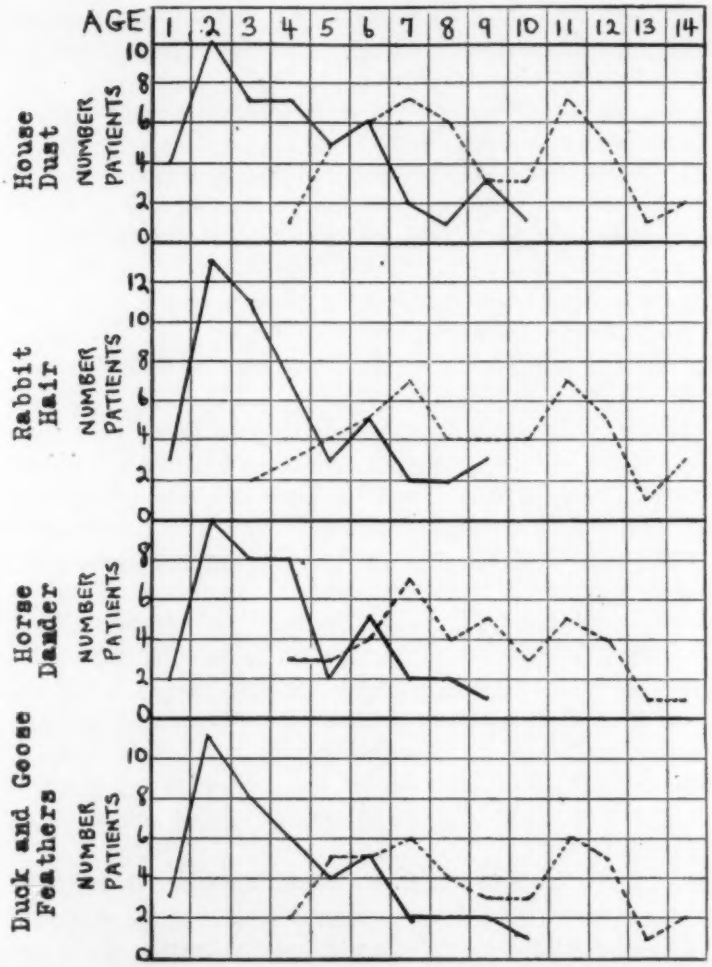

Chart 7.—Showing the most common inhalant positive skin reactions in relation to the age of onset of asthma (plain line), and the age when first seen (broken line).

12. De Besche, A.: Hypersensitiveness and Asthma, Especially in Relation to Emanation from Horses, J. Infect. Dis. **22**:594 (June) 1918.

13. Ratner, B.: Rabbit Hair Asthma in Children, M. Clin. N. Amer. **5**:1129 (Jan.) 1922.

Ratner [14] suggested that rabbit hair should be placed second to horse hair as a causative agent in the epidermal group of asthmas.

Cooke [15] reported an incidence of 5.5 per cent rabbit hair sentizations in 327 patients of all ages.

Herman [8] found eight sensitizations to rabbit hair in twenty-two children, or 36 per cent.

Larsen and Bell,[9] in their series of 100 cases, reported rabbit hair sensitizations in 74 per cent of the protein sensitive group and in 32 per cent of the total series.

Brown,[16] in 100 cases of all ages, reported 10 per cent rabbit hair sensitization as the etiologic factor.

In this series, rabbit hair sensitization was found to occur in 49 per cent of all asthmatic children tested, and in 62 per cent of the protein sensitive group. These figures place rabbit hair sensitization as the most common and important reaction encountered in this class of children in New York City, justifying a detailed study of the rôle this protein plays in the etiology of asthma.

Patients who exhibited a positive skin reaction to rabbit hair were classified into the following five groups:

Group 1.—This group includes only those children with asthma in whom rabbit hair proved to be the sole etiologic factor. Rabbit hair was located in the home of each of these children, and its removal resulted in the complete relief of asthma. Other substances to which the patients reacted were completely disregarded, and no attempt was made to remove the proteins from the patients. In this group, no special instructions were given for house cleaning, and the removal of the rabbit hair itself was sufficient. In view of the fact that I considered all other presenting reactions as potential etiologic factors, after a period of six months the parents were advised of their existence and measures were taken to withdraw the offending proteins from these children. All symptoms of asthma up to this period, however, were still absent.

This group consists of fourteen patients, details of which are set forth in table 4.

It can readily be seen from the preceding table, that pillows and mattresses constitute the primary source of exposure to rabbit hair. In three of these subjects, there was additional exposure in the form of collars and cuffs on the children's coats and in one instance on the coat of a member of the family. These additional exposures to rabbit hair occurred after asthma had already set in.

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14. Ratner, B.: Rabbit Hair Asthma in Children, Am. J. Dis. Child. **24**:346 (Oct.) 1922.

15. Cooke, R. A.: Studies in Specific Hypersensitiveness. IV. New Etiologic Factors in Bronchial Asthma, J. Immunol. **7**:147 (March) 1922.

16. Brown, Aaron: Present Day Treatment of Asthma, New York M. J. **118**:333 (Sept.) 1923.

The relation between the onset of asthma and the duration of exposure to rabbit hair in these children is as follows:

In four patients, asthma occurred soon after exposure, the symptoms persisting from two to four years before the etiology was determined.

In seven patients, exposure continued from one-half to four years before asthma set in. In four of these seven patients, exposure to rabbit hair commenced soon after birth; these patients suffered from asthma for one to nine years, or an average of five and one-half years before the etiology was determined. In case 7, cough set in soon after birth as a result of exposure to a rabbit hair pillow and persisted for one year before asthma appeared.

TABLE 4.—*Group 1. Rabbit Hair, Sole Etiologic Sensitization*

No.	Skin Reaction	Age First Seen	Age of Onset of Asthma	Duration of Exposure to Rabbit Hair	Source of Exposure to Rabbit Hair	Other Positive Skin Reactions
1	+	5	3	2	Mattress	Horse dander, horse serum, duck feathers, dog hair, pea and wheat globulin
2	++	8	4	4	Pillow	Wheat globulin and herring
3	++	8½	3	8	Pillow	Horse dander, sheep wool, chicken feathers, goat, cat and cattle hair, lactalbumin and lettuce
4	+++	7½	5½	3	Mattress, pillow	House dust, horse dander, sheep wool, duck feathers, goat and dog hair, staphylococcus pyogenes aureus, coffee, lettuce, radish, cucumber
5	+++	11	4	11	Pillow	Dust, horse dander, dog and goat hair, cucumber, cabbage and coffee
6	+++	9	3	4	Mattress, pillow	Horse dander, sheep wool, orris root, dog, camel and goat hair and coffee
7	+++	10	1	10	Pillow	Dust, duck feathers, potato
8	+++	11	2	11	Pillow	Dust, horse dander, duck feathers, cat hair, wheat globulin, proteose and leucosin, barley, pike, micrococcus catarrhalis
9	+++	7	2	7	Pillow	Horse dander and duck feathers
10	+++	12	6	3	Mattress, pillow	House dust, horse dander, duck feathers, orris root, goat hair, coffee, lettuce and cucumber
11	+++	8	4	4	Pillow	Dust, horse dander, orris root, duck feathers, goat hair, whole wheat, wheat globulin, coffee, corn, cucumber, lettuce, radish and pineapple
12	+++	3½	2½	3	Pillow	Cat hair and lettuce
13	++++	5	1½	¾	Pillow	Dust, duck and chicken feathers, wheat globulin, coffee, veal and peas
14	++++	4½	3	1½	Pillow	Goat hair, coffee, cucumber, lettuce

In three patients, exposure to rabbit hair occurred after the onset of asthma. The exact etiology prior to the exposure to rabbit hair could not be determined; however, the fact remains that at the time these patients were examined the sole etiologic factor was unquestionably rabbit hair. In Case 13, symptoms of asthmatic bronchitis followed pneumonia at the age of 1½ years, but definite bronchospasms did not set in until about the age of 4½ years, two months after exposure to a rabbit hair pillow. In case 6, asthmatic symptoms were present for two years before contact with rabbit hair took place, and exposure persisted for the following four years before it was determined that

rabbit hair was the sole existing etiologic factor. It is highly probable that sensitizations were responsible for the earlier asthmatic manifestations. In case 10, asthma was present for three years before exposure, and persisted for another three years before rabbit hair was determined as the current etiologic factor.

It will be noted that all of these patients were sensitive to other proteins. In the absence of exposure to rabbit hair, I am firmly convinced, after many observations, that these concurrent sensitizations play no part in the production of symptoms. The exception to this was case 2, in whom the ingestion of herring caused a spasmodic cough. With the existence of exposure to rabbit hair, these concurrent sensitizations were instrumental in aggravating and prolonging the condition. With the removal of the rabbit hair, the most toxic of these proteins, the tolerance of the patient is so raised that these secondary protein sensitizations are no longer capable of producing irritation. As an instance of this fact, the well-known observation might be stated that patients suffering with hay-fever and also sensitive to proteins other than pollen, cannot tolerate these substances during the pollenating season. At any other time, these secondary protein sensitizations do not cause symptoms.

That this group is an important one, is evidenced by the fact that it represents 18 per cent of the protein sensitive group and 14 per cent of the entire series.

Group 2.—In this group, rabbit hair sensitization is only one factor in the causation of asthma. The other etiologic sensitizations varied greatly and included all protein groups. Table 5 is a summary of this group.

It will be noted that rabbit hair pillows and mattresses comprise the most important source of exposure to this group of cases also. Furthermore, three of these patients were exposed to additional sources, such as collar and cuffs on the patients' coats, or coats worn by members of the family. In one instance (case 30), although the child had slept on a rabbit hair pillow since birth (two years), the first attack of asthma followed direct exposure to a live rabbit. In three others (cases 18, 27 and 28) of this group, asthma was aggravated by exposure to live rabbits. These patients had asthma for four years, six years and two months, respectively, before rabbit hair was discovered as one of the etiologic factors.

In ten cases, exposure to rabbit hair ranged from one-half to three and one-half years prior to the onset of asthma; and in three of these exposure to rabbit hair commenced within the first months of life, asthma setting in from one and one-half to two years after exposure. These patients had asthma from one to nine and one-half years before rabbit hair was found to be one of the etiologic factors in asthma.

TABLE 5.—*Group 2. Rabbit Hair Sensitization. One of Various Causes of Asthma*

No.	Skin Reaction	Age First Seen	Age of Onset of Asthma	Exposure to Rabbit Hair	Source of Exposure to Rabbit Hair	Other Etiologic Sensitizations and Current Factors	Protein Sensitizations Other than Rabbit Hair
15	±	7	5	5	Pillow	Bacterial	Dust
16	±	5½	1½	5½	Mattress	Dust, horse dander, egg, fish, ragweed	Dust, horse dander, duck feathers, orris root, ragweed, timothy, whole egg, egg white, egg yolk, barley, beet, lima bean, mustard, radish, almond, herring, pike, salmon, smelts, mackerel, haddock
17	+	5½	3½	1	Pillow	Duck and goose feathers, potato, fish	Horse dander, duck, goose and chicken feathers, cat hair, sheep wool, whole egg, milk lactalbumin, lamb, beet, potato, herring, pike, salmon, smelts, bluefish, butterfish, halibut, clam, crab, oyster, lobster, brazil nut and strawberry
18	+	8	2	6	Pillow	Food and ragweed	Dust, horse dander, whole egg, egg white, egg yolk, cheese, corn, barley, beef, chicken, veal, lamb, potato, radish, herring, pike, salmon, smelts, brazil nut, ragweed and orchard grass
19	++	6	3	5	Pillow	Duck feathers and foods	Dust, horse dander, duck and goose feathers, milk, casein, lactalbumin, cheese, whole wheat, wheat globulin, rice, rye, coffee, beef, almond, strawberry
20	++	7	4	2	Pillow, mattress	Bacterial	Horse dander, goat hair, camel hair and coffee
21	++	12	2	12	Pillow	Duck feathers, bacterial	Dust, horse dander, duck feathers, dog hair and coffee
22	++	3	2	3	Pillow	Chicken feathers, cat hair, egg, meats, ragweed	Chicken feathers, cat hair, whole egg, egg white, egg yolk, lactalbumin, beef, chicken, veal, lamb, goose, mustard, radish, brazil nut, ragweed, red-top
23	++	10	9	3	Pillow	Ragweed	Cat and goat hair, lettuce, ragweed
24	+++	14	4½	13	Pillow	Horse dander	Horse dander, cat and goat hair, cabbage, radish and lettuce
25	+++	11	2	¾	Pillow	Ragweed	Lettuce and ragweed
26	+++	8½	6	3	Collar, cuffs	Foods	Dust, horse dander, duck and goose feathers, whole egg, egg white, egg yolk, wheat proteose, wheat leucosin, coffee, barley, radish, almond, tomato, pike, smelts, salmon, ragweed, mackerel, brazil nut
27	++++	6½	2½	4	Pillow	Dust and duck feathers	Dust, horse dander, duck feathers and coffee
28	++++	4	3¾	4	Pillow	Horse dander, feathers	Horse dander, duck and goose feathers, dog hair, orris root, lactalbumin, corn, rice, barley, oat, carrot, onion, radish, tomato, rhubarb
29	++++	13½	9	6	Pillow	Duck feathers	Dust, duck feathers and goat hair
30	++++	6½	2	6½	Pillow	Dog and cat hair	Horse dander, dog, cat, goat and camel hair, sheep wool, wheat and cucumber
31	++++	11	5	7	Pillow	Horse dander, and goose feathers	Horse dander, goose feathers, coffee, rice and barley

In the remaining three of this group (cases 17, 20 and 25), exposure to rabbit hair occurred after the onset of asthma. These patients presented symptoms from one to nine years before exposure to rabbit hair occurred. That other proteins were responsible for inducing the onset of asthma in these cases is highly probable. How soon after exposure rabbit hair began to operate as a contributory factor cannot be definitely determined. This and many other such observations to which reference will be made, demonstrate that additional etiologic protein sensitizations can be developed after asthma is already well established. This fact is of practical importance, and should be borne in mind in the management of the case.

TABLE 6.—*Group 3. Rabbit Hair Sensitization—A Previous but not a Current Etiologic Factor Because of Freedom from Exposure*

No.	Skin Reaction	Age First Seen	Age of Onset of Asthma	Freedom from Exposure to Rabbit Hair	Source and Duration of Exposure to Rabbit Hair	Current Etiologic Factors	Protein Sensitizations Other Than Rabbit Hair
32	±	4	2	3¾	Live rabbit, 4 mo.	Dust, feathers, horse dander, ragweed	House dust, duck and goose feathers, horse dander, ragweed, cat hair, sheep wool, orris root, whole wheat, wheat proteose, rice, barley, radish and rhubarb
33	++	6½	3½	2¾	Felt hat, fur trimmed, 4 mo.	Duck and goose feathers, potato	Dust, horse dander, duck feathers, cat hair, goose and potato
34	++++	7½	5½	2¼	Live rabbit, 5 mo.	Foods	Dust, horse serum, cat hair, lactalbumin, cheese, rice, beef, chicken, lamb, veal, goose, brazil nut, herring, pike, salmon, smelts, bluefish, mackerel, perch, codfish and haddock

This group accounts for 24 per cent of those sensitive to protein or 17 per cent of the entire series of cases.

Group 3.—In this group, rabbit hair at one time played a part in the causation of asthma, but was not a factor in the current etiology. These patients had not been exposed to rabbit hair for a period varying from two to four years. The current etiologic sensitizations of this group are shown in table 6.

It is of interest to note that two subjects (cases 32 and 34) were exposed to live rabbits for one and three months, respectively, before symptoms of asthma occurred. One subject (case 33) wore a hat trimmed with rabbit fur one month before symptoms began. These patients had asthma for two to three years before they came under observation. This group represents 4 per cent of the protein sensitive, or 3 per cent of the entire series.

Group 4.—In this group, rabbit hair, though present, played no part either in the previous or current etiology, in spite of the fact that exposure to rabbit hair was demonstrated in each case. The etiologic factors are shown in table 7.

TABLE 7.—*Group 4. Rabbit Hair Sensitization with Exposure Playing no Part in the Etiology*

No.	Skin Reaction	Age First Seen	Age of Onset of Asthma	Exposure to Rabbit Hair	Source of Exposure to Rabbit Hair	Etiologic and Other Current Factors	Protein Sensitizations Other Than Rabbit Hair
35	±	6	2½	6	Pillow	Dust, bacterial	Dust, duck and goose feathers, whole egg, wheat globulin
36	±	10	2	½	Pillow	Inhalants, healed pulmonary lesions	Dust, horse dander, duck feathers, cat, dog and camel hair
37	±	11	1	4	Mattress	Duck feathers	Dust, horse dander, duck feathers, almond
38	++++	13	8	4	Coat collar	Inhalants, endocrine dysfunction	Dust, horse dander, duck and goose feathers, cat, goat, camel hair, canteloupe

TABLE 8.—*Group 5. Rabbit Hair Sensitization, with no History of Exposure and Apparently not a Factor in the Etiology*

No.	Skin Reaction	Age First Seen	Age Onset Asthma	Etiologic and Other Current Factors	Protein Sensitizations Other Than Rabbit Hair
39	±	7	2½	Dust, chronic bronchitis, emphysema	Dust, horse dander, duck feathers, dog hair, pea and ragweed
40	±	5	2	Horse dander, eggs	Dust, horse dander, orris root, duck feathers, whole egg, egg white, egg yolk, lactalbumin, rhubarb
41	+	14	3	Dust, duck feathers, chronic bronchitis and emphysema	Dust, duck feathers, orris root
42	+	6	6	Foods	Horse dander, chicken feathers, cat and dog hair, whole egg, egg white, buckwheat, tea, asparagus, cucumber, chestnut
43	+	11	7	Dust, goose feathers	Dust, goose feathers and cat hair
44	+	11	7	Ragweed, timothy, horse dander	Horse dander, horse serum, cat, dog and camel hair, rye, carrot, ragweed, timothy
45	++	12	6	Chronic bronchitis, emphysema	Dust and duck feathers
46	++	12	2	Goat hair	Horse dander, goose feathers, goat hair, cucumber
47	++++	9	7½	Horse dander, chronic bronchitis, emphysema	Horse dander, duck and goose feathers, wheat globulin, coffee, rice, radish, pike, bacillus coli
48	++++	10	1	Chronic bronchitis, emphysema	Horse dander, goose feathers, cat hair, wheat globulin, rice, cucumber, lettuce, potato, radish
49	++++	5	1½	.....	Horse dander, cat and cattle hair, whole wheat

This group represents 5 per cent of the protein sensitive, or 4 per cent of the entire series of cases.

Group 5.—In this group, exposure to rabbit hair in any form or at any time could not be demonstrated, and yet definite positive reactions occurred, about 30 per cent being as large as four plus reactions. The etiologic and other current factors are shown in table 8.

While the history of exposure to rabbit hair was negative, yet it is more than reasonable to assume, in face of the widespread usage of the hair, that these patients were exposed at some time or other during their lives to account for the sensitization being present.

This group represents 22 per cent of all patients sensitive to rabbit hair, 14 per cent of the total protein sensitive cases or 11 per cent of the entire series.

COMMENT

In this series, the frequency of occurrence of rabbit hair sensitization in children is impressive. A proper interpretation of these reactions is rather important, since, as is demonstrated in these five groups, the rôle of rabbit hair sensitization in the etiology of asthma is quite variable.

This is the first attempt to determine the proper rôle that rabbit hair plays in asthma in children. It cannot be too strongly emphasized that the exact rôle that rabbit hair plays in the sensitive person is not determined by the size of the cutaneous reaction, but rather by the effect of accidental or persistent contact with rabbit hair and the subsequent removal from the patient's environment. In some of the complex multiple protein sensitive cases, hospitalization had to be resorted to before the rôle of rabbit hair could be determined definitely.

In six cases, exposure to rabbit hair occurred after the onset of asthma from other causes. That these cases are examples of acquired rabbit hair sensitization is strongly suggestive. The newly acquired rabbit hair sensitization was later recognized as being responsible for the persistence and aggravation of the existing asthma.

In other cases, rabbit sensitization appeared to be an etiologic factor at the onset of asthma, but after several years, due to other sensitizations, rabbit hair only assumed a contributory rôle, as was demonstrated by the fact that the removal of the rabbit hair from the patient's environment only partially relieved the symptoms.

To ascertain the source of exposure to rabbit hair, search should be made in the patient's home. A history carefully and patiently taken is of assistance in revealing previous exposure. One child slept on a pillow from which rabbit hair had been emptied some years previously and replaced with duck feathers. On examination, the corners and the entire under surface of the pillow cover contained rabbit hair. Complete relief followed removal of this pillow, although the child slept after that on an unadultered feather pillow. Although the child's own home is the most frequent source of exposure, it must be borne in mind that he may be exposed to rabbit hair in other places. This would possibly account for the group of cases in which a history of exposure could not be elicited. Changing environment has been responsible for a recurrence of bronchospasms after freedom from asthma for over one

year. This has been well illustrated by several patients who went to the Catskill Mountains during the summer vacation period, asthma occurring after the first or second night, which persisted until it was discovered that the patients were sleeping on a rabbit hair mattress or pillow, the removal of which rendered the patients free from symptoms. Formerly, the return of asthma under such conditions would have been attributed to "altitude" or "that the air was too strong."

The most frequent source of exposure to rabbit hair was found in the pillows and mattresses on which the patients slept. However, articles of apparel trimmed with rabbit hair, felt hats, fur coats and toy animals are additional sources of exposure. It must be remembered that rabbit hair workers may bring sufficient hair home on their unbrushed clothes to cause symptoms in a sensitive individual.

The severity of the asthmatic symptoms as a result of exposure to rabbit hair varies widely, and depends on the individual. It has been stated by Walker,[17] Piness,[18] and others, that a sensitive person continually exposed to an etiologic inhalant has asthma throughout the entire year. This conception does not harmonize with the clinical facts of this study. In one family there were two asthmatic children who slept together, and therefore both were subject to the same rabbit hair exposure. One had frequent attacks of asthma; the attacks in the other occurred at intervals of three to nine months. In this case the severity and the onset were controlled by the incidence of concomitant upper respiratory infection. Both patients showed no symptoms between attacks. The removal of the pillows, mattresses and fur trimmings from the home resulted in freedom from asthma for both for more than two years at the time of writing.

In some cases the onset of asthma is preceded for a year or more by a "recurrent cough," "rhinitis" or "conjunctivitis," particularly on arising in the morning. These conditions resist all treatment. After the asthmatic condition is studied, and the etiologic allergic nature is brought to light, with the relief of the asthma, these conditions also disappear.

The tolerance of sensitive persons to rabbit hair (and all other sensitizations) varies widely. Some children develop asthma immediately or shortly after exposure, while others do not manifest symptoms until one-half to four years have elapsed. Because this tolerance is so variable, asthma is remittent or intermittent. Other factors have a marked influence on tolerance, such as intercurrent diseases or infections. The degree of a patient's susceptibility is dependent on his tolerance. Tolerance to a protein cannot be measured. It is a term employed and understood only in the language of the clinician.

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17. Walker, I. C.: Oxford Medicine, New York, Oxford Press, 1920.

18. Piness, G.: Etiology of One Hundred Fifty Cases of Bronchial Asthma, California State J. Med. **19**:29 (Jan.) 1921.

SENSITIZATION TO HORSE DANDER

Sensitiveness to horse dander was found to occur in 50 per cent of the protein sensitive group and to 40 per cent of the entire series, and ranks fourth in the inhalant group in frequency of occurrence. However, as an etiologic sensitization, horse dander accounts for only 10 per cent of the protein sensitive asthma cases, and in none was horse dander solely responsible for the asthma.

In the majority of these subjects, the source of exposure to horse dander cannot be found in their homes. A few patients lived in the immediate vicinity of a stable; in a few others, exposure was found in a mattress and chair, stuffed with unsterilized horse hair.

The association of rabbit hair and horse dander sensitizations in the same patient is of such frequent occurrence as to warrant investigation.

TABLE 9.—*The Relationship Between Rabbit Hair and Horse Dander Occurring in the Same Patient*

Reaction	Group * 1 RH	1 HD	2 RH	2 HD	3 RH	3 HD	4 RH	4 HD	5 RH	5 HD	Total RH	Total HD
∓	0	2	1	3	1	2	2	1	2	1	6	9
+	1	2	2	2	0	0	0	2	2	3	5	9
++	1	1	3	2	1	0	0	0	1	1	6	4
+++	4	1	2	2	0	0	0	0	0	0	6	3
++++	3	3	4	3	0	0	1	0	3	3	11	9
Number of patients reacting to rabbit hair and horse dander	9		12		2		3		8		34	
Total patients sensitive to rabbit hair	14		17		3		4		11		49	
Number of patients in whom horse dander was an etiologic factor	0		4		1		0		3		8	

* The groups as designated have reference to the rabbit hair sensitization groups as outlined in tables 4 to 8 inclusive. RH = rabbit hair; HD = horse dander.

It will be observed that the curves representing rabbit hair and horse dander sensitizations (chart 7) are essentially the same in contour. The number of patients reacting to both rabbit hair and horse dander are thirty-four, or 43 per cent of the protein sensitive patients. Thus, horse dander sensitization alone occurred in six cases.

In order to study the significant relationship between these two sensitizing proteins, the five groups sensitive to rabbit hair (tables 4 to 8 inclusive) were used. The results are found in table 9.

The incidence of horse dander sensitizations in each of the five groups sensitive to rabbit hair is quite proportionately distributed.

In group 1, in which rabbit hair was the sole etiologic factor, nine, or 64 per cent, of these fourteen patients also reacted to horse dander.

In group 2, in which rabbit hair was only a contributory etiologic factor, twelve, or 70 per cent, of these patients also reacted to horse dander, four of which also took part in the causation of asthma.

Of the remaining groups in which rabbit hair did not enter into the existing etiology of asthma, four of the thirteen patients reacting to horse dander were etiologically sensitive.

Thus, of the eight etiologic horse dander sensitizations, there were 3 plus minus, 1 one plus, 1 two plus, 1 three plus and 3 four plus reactions, which again illustrates my contention that it is not the size of the reaction that determines the rôle that any protein may play in asthma.

Of the thirty-four patients reacting to both rabbit hair and horse dander, rabbit hair is wholly or partially responsible for asthma symptoms in twenty-one while horse dander accounts for only eight patients; thus definitely showing that asthma caused by rabbit hair is three times as frequent as asthma caused by horse dander. Since the relative frequency of rabbit hair and horse dander sensitizations are approximately the same, it is reasonable to conclude, all things being equal, that the toxicity of rabbit hair protein is far greater than that of horse dander. It is possible to advance the claim that since these patients are not exposed to horse dander as frequently and continuously as they are to rabbit hair, the greater toxicity of the latter is therefore only relative. This is not substantiated by clinical experience.

Of the six patients sensitive to horse dander not exhibiting rabbit hair sensitization, in only one is horse dander an etiologic sensitization.

SENSITIZATION TO HOUSE DUST

The discovery of house dust as a specific factor in asthma must be credited to Cooke,[15] who demonstrated the specific nature of dust by the cutaneous test. He observed sensitiveness to house dust in persons who failed to react to any other proteins.

Leopold and Leopold [19] made a study of the effect of introducing house dust into the environment of a patient shown by test to be sensitive to an extract of the identical dust. A specially constructed room was installed in the Hospital of the University of Pennsylvania, in which it was possible to observe patients under controlled conditions of environment, in relation to the presence and quantity of specificially allergic inhalation substances. Their experiments seem to indicate that it is possible by means of their equipment to render a room relatively dust free, sufficient to keep a patient suffering with asthma from dust free of asthmatic symptoms. They concluded that it seems evident that house dust contains one or more specifically allergic substances capable of producing an immediate general reaction, and that this reaction cannot be explained on the basis of mechanical irritation, thus confirming the opinion held by Cooke.

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19. Leopold, S. S., and Leopold, C. S.: Bronchial Asthma and Allied Allergic Disorders: Preliminary Report of a Study Under Controlled Conditions of Environment, Temperature and Humidity, J. A. M. A. **84**:731 (March 7) 1925.

Experimentally, Spivacke and Grove [20] demonstrated a specific excitant of atopy (allergy) in the blood of a person sensitive to dust, a specific reagin with which a normal skin site could be sensitized to the dust atopen (allergen), after the method of local passive transfer of Prausnitz and Küster. With this method, results were obtained which would indicate the existence of more than one dust atopen.

Recently, Grove and Coca [21] have concluded that the substance in house dust extract which is responsible for the cutaneous reaction seems not to be protein in character, because after all proteins and other detectable nitrogenous substances from the house dust extract were removed by means of tryptic digestion and dialysis, there occurred no appreciable lessening of the atopic (allergic) activity of the extracts.

The house dust used in this series consisted of three powdered extracts prepared from the dusts from three separate homes. All the patients were tested with all three extracts. Most patients reacted to at least two of the three extracts; few only to one. The dust giving the maximum skin reaction was the only one recorded. The incidence of house dust sensitization would probably have been greater if an extract had been made from the home of each individual patient. This was not attempted because of the many difficulties involved. An active polyvalent stock house dust extract would also have given a somewhat higher percentage of positive reactions than the three dusts used. This was clearly demonstrated in a later comparative study.

My clinical experience has verified Cooke's statement, that the sensitizing atopen in house dust does not depend on the presence of other inhalant substances which may be in the house.

Forty-six patients, or 58 per cent of the protein sensitive group and 46 per cent of the entire series, gave positive skin reactions to house dust as follows: 16 plus minus, 17 plus, 6 two plus, 3 three plus and 4 four plus reactions. Cooke,[15] dealing with all ages, reported an incidence of 33 per cent of house dust sensitization.

House dust sensitization is one of the most common reactions met, and its importance cannot be minimized, but as an etiologic factor of asthma, at least in children, it is not so great as reports in the literature would lead one to believe. As a matter of fact the etiologic rôle of dust sensitization has been over-emphasized. In this series it was found that house dust really played a lesser rôle than rabbit hair in the causation of asthma. In many instances in which house dust and rabbit hair

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20. Spivacke, C. A., and Grove, Ella F.: Studies in Specific Hypersensitiveness. XIV. A Study of House Dust Atopen in Asthma, J. Immunol. **10**:465 (March) 1925.

21. Grove, Ella F., and Coca, A. F.: Studies in Specific Hypersensitiveness. XV. On the Nature of the Atopens of Pollen, Horse Dander and Green Pea, J. Immunol. **10**:471 (March) 1925.

reactions were both present, the house dust reaction was ignored and the patients recovered with the removal of the rabbit hair alone. However, there is a small group of patients in whom dust plays a definite etiologic rôle, to the extent that the recovery or improvement from asthma directly depends on the treatment with the extract or the removal of the patient from the unfavorable environment.

The only accurate way of determining the exact rôle of house dust sensitization is by some such method as used by Leopold and Leopold [19] at the University of Pennsylvania; since I did not have such advantages, it is very difficult to evaluate house dust in this series. Purely from a clinical point of view, my impression is that in approximately 20 per cent of this series, house dust played either a direct or indirect rôle in the etiology. The incidence of house dust sensitizations in this series will be found in table 3.

SENSITIZATION TO FEATHERS

Of the feather sensitizations, reactions were found to duck, goose and chicken. Duck and goose feathers were the most common. Since duck and goose feathers were found so frequently mixed in the pillows of these children, it was found best to consider these two as if representing one protein. Forty-four patients reacted to either one or both, representing 56 per cent of the allergic group and 44 per cent of the entire series. Chicken feather reactions occurred comparatively infrequently, in only 7 per cent of the protein sensitive group and in 6 per cent of the total cases. Over 30 per cent of these also reacted to duck and goose feathers.

The feather sensitizations seem to play mostly a contributory rôle in the etiology of asthma. In only a very small percentage (from 2 to 3 per cent) were these the sole etiologic factor.

Ninety-two per cent of this series were Jewish children. Chicken feather pillows and comforters are rarely used in the Jewish homes. This accounts probably for the relative infrequency and unimportance of this inhalant in this and in other series.[22]

SENSITIZATION TO OTHER INHALANTS

The remaining inhalent sensitizations (excluding pollen) are grouped together because they almost always occurred in conjunction with one or more of the more important inhalant substances. The incidence of these minor inhalants in the entire series were as follows: cat hair, 24 per cent; goat hair, 16 per cent; dog hair, 13 per cent; orris root, 12 per cent; sheep wool, 10 per cent; camel hair, 8 per cent, and

22. Peshkin, M. M.: The Significance of the Protein Skin Reactions in Bronchial Asthma, New York M. J. **117**:88 (Jan. 17) 1923.

cattle hair, 4 per cent. These sensitizations either acted in a contributory capacity, or most often, with the exception of cat and dog hair, played no existing etiologic rôle whatsoever.

In considering the importance of orris root as an etiologic factor in rhinorrhea and asthma in adults, it is interesting to note its complete unimportance as a causative factor in infants and in children. The exposure of children to orris root is in direct proportion to the amount of powders and cosmetics their mothers use. Perhaps this observation is due to the fact that the adult members of the families of this particular group did not use cosmetics and face powders to any considerable extent. I have no data on this point, but if they do use cosmetics as much as other classes, it would be an indication that perhaps orris root is a sensitization which is acquired in adult life.

I am of the impression that the camel hair reactions here recorded are due to some irritating substance contained in the testing material, and is, therefore, viewed with suspicion as being an irritative or nonspecific reaction. This irritating quality I have also found in tuna fish extract, which gives a positive reaction in every person tested, for which reason this substance was not included among the proteins of this study. Corn pollen also seems to contain an irritating substance which is responsible for frequent skin reactions.

Due to the relative frequency of reactions to the minor inhalants, and to the fact that any secondary reaction may be a contributory factor in either prolonging or aggravating symptoms, they should not be ignored, particularly since they lend themselves so readily to removal from the patient's environment.

SENSITIZATION TO POLLEN

All patients were tested in a routine manner with the important wind and insect borne pollens. In this series, only ragweed, timothy, redtop, orchard and June grasses were included in the statistical report. Ragweed sensitization represents the short and tall varieties. In no instance did tall ragweed sensitization occur without a concomitant short ragweed reaction.

Whenever the etiology of asthma was obscure, and a history suggested possible pollen etiology and the cutaneous test was negative, the conjunctival test was employed. The pollens employed for these tests were in dry powdered form and were highly potent.

In children, when the history indicates a true pollen sensitization, either by the onset of asthma during the season or following hay-fever, and positive reactions obtained, it is no indication that pollen is the sole causative factor. In this series, in fact, the observation has been made that almost invariably other protein sensitizations played an important

rôle in the production of symptoms. In this particular group it was the rule to find a multiplicity of reactions. For this reason all children giving a history of what is seemingly only a pollen asthma, should be tested in a routine manner with the entire set of the common food and inhalant proteins. When children present themselves with simple hay-fever, it is my practice now to test them with all proteins.

Twenty patients, or 25 per cent of the protein sensitive group, reacted to one or more of the before-mentioned pollens. The details of these sensitizations are set forth in table 10.

Of the twenty patients, seventeen showed positive ragweed reactions as follows: etiologic reactions, skin 8 and conjunctival 3, total 11;

TABLE 10.—*Sensitization to Pollens in Children with Asthma*

Number	Age	Ragweed	Timothy	Redtop	Orchard Grass	June Grass
1	11	c—	c—	c++*	c+*	c—
2	8	c++*	c+*	c—	c—	c—
3	10	c+++*	—	—	—	—
4	11	c++++*	—	—	—	—
5	4	±*	—	—	—	—
6	7	++*	—	—	—	—
7	11	+*	c+*	—	—	—
8	8	+*	—	—	+	—
9	11½	+*	±	—	—	—
10	9	±*	—	—	—	±
11	3	++*	—	±	—	—
12	11	±*	—	—	—	—
13	8½	+	—	—	—	—
14	4	—	—	—	c±	c+
15	4½	c±	c—	c—	c—	c—
16	6½	c—	c+	c+	c+	c++
17	7	++	—	—	—	—
18	5	+	±	±	+	+
19	10	c±	c—	c—	c—	c—
20	9	+	—	—	—	—
Etiologic conjunctival sensitization		3	2	1	1	0
Etiologic cutaneous sensitization		8	0	0	0	0
Total etiologic sensitizations		11	2	1	1	0
Nonetiologic conjunctival sensitization		2	1	1	2	2
Nonetiologic cutaneous sensitization		4	2	2	2	2
Total nonetiologic sensitizations		6	3	3	4	4
Total number etiologic and nonetiologic conjunctival and cutaneous sensitizations		17	5	4	5	4

* The asterisks designate etiologic sensitizations. Conjunctival test, c; plus minus, ±; one plus, +; two plus, ++; three plus, +++; four plus, ++++; negative reaction, —.

nonetiologic reactions, skin 4 and conjunctival 2, total 6. Seven of these seventeen patients also reacted to one or more of the grasses; only two exhibited etiologic sensitizations to timothy.

Of the twenty patients, ten showed positive grass reactions of whom only three were etiologically sensitive. Two of the three patients were associated with late hay-fever. The remaining one (case 1) was conjunctival sensitive only to redtop and June grass.

Thus, in only twelve of the twenty patients sensitive to pollen, did pollen enter as one of the etiologic factors in asthma. Eleven of these twelve patients were sensitive to ragweed. Two of these subjects had early and late hay-fever asthma. The remaining case presented the interesting sensitizations to red-top and June grass, which will be dis-

cussed in detail. It will be noted that three of the twelve patients gave ragweed plus-minus cutaneous reactions, which again emphasizes the etiologic importance of these so-called plus-minus or doubtful reactions.

Eight patients, or 10 per cent of the protein sensitive group, show reactions to pollens (ragweed being four times more frequent than timothy) which do not enter into the etiology of asthma or hay-fever. Four per cent of the subjects, or 5 per cent of the allergic group, who are etiologically sensitive to ragweed also give a cutaneous reaction to either timothy, redtop, June or orchard grass, which were not etiologically active.

Why nine of twenty patients proved to be refractory to the cutaneous pollen test, although positive to the conjunctival test, is a question that I cannot answer. All of these patients gave positive cutaneous reactions to other proteins, done at the same time, which in each case entered into the etiology of asthma. In only five of these nine cases, the pollen sensitizations elicited by conjunctival test coincided with a pollen etiology.

Kahn and Grothaus [23] report fifteen cases (13 per cent of their series of 115 patients with hay-fever and asthma, of all ages) with repeated negative pollen skin tests, but all of which gave histories consistent with a pollen etiology. Eight of these subjects were negative to all proteins employed in routine testing. They used the intradermic test with 0.01 cc. pollen extract (66.6 per cent glycerine, 33.3 per cent Coca's solution) routinely with dilutions of 1:5,000, 1:500, 1:50, and 1:20 when previous weaker solutions were negative. All of these fifteen patients were treated empirically with pollen extracts. Much to their surprise, all gave definite local, and occasionally constitutional reactions at various times during the treatment. As a result, five of these patients were free from symptoms, six others improved and four only failed to show any improvement. As a result of this experience, they recommend that in the absence of positive skin tests and when the history gives the slightest indication of trouble during the pollinating seasons, irrespective of food or inhalant sensitizations, all such subjects should be tested with the following pollen extract dosages subcutaneously: 1:5,000, 0.05 cc; 1:500, 0.05 cc; 1:50, 0.05, 0.1, 0.2 cc.; 1:20, 0.05, 0.1, 0.15, 0.2 cc., often getting positive reactions with as low as the 1:500 dilution. In no case should the subject be considered negative to pollen unless the maximum dose mentioned could be tolerated without reaction. These hypodermic tests are given one each day until a reaction is obtained. They had no experience with the ophthalmic tests. They state that "the pollen skin tests are not to be considered

23. Kahn, I. S., and Grothaus, E. M.: Studies in Pollen Sensitiveness, M. J. & Rec. **121**:664 (June 3) 1925.

absolutely diagnostically dependable," a conclusion which I reached in 1922, but I am unalterably opposed to any diagnostic method involving test injections of any foreign substance. According to this method, it requires from one to nine days to make a diagnosis. Nonspecific local reactions are common to any injection of any protein substance. There is also danger of inducing constitutional reactions either by overdosage or by accidental entry into the circulation. All of these objections can be overcome by the simple and harmless conjunctival test previously described, a positive diagnosis being objectively made within a few minutes.

The following is a case report of a patient, with asthma occurring in early hay-fever in whom the pollens were positive only to the conjunctival test. There is another interesting point in connection with this case. It is generally accepted that the most common primary cause of early hay-fever is timothy, and also that in the experience of most workers that early pollen cases react to the entire biologic group. In this case the reactions by the conjunctival test were positive only to red-top and orchards grass, two of the minor causative factors in this locality. This report is given in detail to illustrate the method of history taking as well as to point some interesting features.

CASE REPORT

F. E., a girl, aged 11 years, was first seen on March 23, 1922.

Past History.—The patient was breast fed for nine months. There was no history of "recurrent bronchitis," "rhinitis" or vomiting, and no skin lesions of any sort. The onset of asthma was sudden; the season of the year could not be remembered. At 1 year of age (1911) the condition was associated with vomiting and fever. From the beginning, attacks occurred about every two weeks throughout the year, and lasted for two days to one week. Each attack was associated with fever and vomiting until 1918, when the patient was 7 years of age, and when the asthma ceased entirely. She remained free from symptoms until the age of 9 (1920), when the asthmatic attacks recurred at monthly intervals and were associated with vomiting but no fever. In 1921, she left her home in Russia and came to New York; in May she began to have rhinorrhea, and in June severe conjunctivitis with photophobia developed, which was diagnosed as vernal catarrh; this lasted until the following winter. When she lived in Europe she rarely complained of "running of the eyes and nose."

While in Europe there was no intolerance noticed to any special substance. While in New York, after the first vernal catarrh season, she developed a noticeable intolerance for soap, smoke, dust, foul odors, gasoline, variations of weather conditions and a susceptibility to upper respiratory infections. Measles and pertussis occurred when she was 9 years of age. What effect these intercurrent diseases had on the return of asthma could not be ascertained.

Family History.—A maternal great aunt had asthma, otherwise the history was negative.

Appearance at Examination.—The patient coughed mostly during the night; the sputum was scant and there was a watery nasal discharge. The throat felt dry. There was dyspnea on and off. The child slept poorly. The bowels were irregular; there were no pain or headaches. She ate freely of delicatessen and other spiced foods.

Summary and Comment.—The child maintained that, up to the age of 7 years (1918), she always observed several worms in the vomitus and insists some of these were alive, and when expelled caused choking sensation. About this time the vomiting ceased entirely and the asthma was absent for two years. The possibility of worms being one of the causes of asthma cannot be entirely excluded, especially when fever was associated with each attack in the earlier years of childhood. However, the interesting feature of this case is the symptoms of early hay-fever and conjunctival symptoms strongly suggestive of vernal catarrh since coming to New York from her home abroad, and the subsequent intolerance to many irritating nonspecific factors coupled with an acquired susceptibility to upper respiratory infections. Thus it appears that the causes for the previous asthma and the existing seasonal nasal and eye symptoms are entirely independent of each other.

Physical examination was negative except for hypertrophic tonsils, and the usual asthmatic lung findings.

Roentgenoscopy of the chest and nasal accessary sinuses was negative. The Pirquet reaction was moderately positive and the cutaneous protein tests were negative except for definitely delayed positive reactions to *Streptococcus hemolyticus,* Friedländer's bacillus, *Bacillus coli* and *Micrococcus catarrhalis.*

Subsequent History.—On April 11, 1922, vaccine therapy was commenced. A vaccine consisting of *Streptococcus hemolyticus* and Friedländer's bacillus was used, which was discontinued on October 17. The asthmatic condition was much improved under vaccine therapy. The hay-fever symptoms were less in severity as compared with the previous year. On May 20, the patient presented a typical picture of early hay-fever. The cutaneous pollen tests were performed on this date with negative results, and at the end of the season they were again negative. In 1923, the conjunctival tests with natural pollen gave reactions to red-top and orchard grass. Preseasonal treatment with extracts of red-top and orchard grass was instituted. With the exception of several days of hay-fever, the child was quite free from symptoms throughout the season. Similar treatment was carried out in 1924 and 1925, with almost complete relief of all symptoms. The last attack of asthma occurred in April, 1924. On July 2, 1925, the cutaneous tests for timothy, red-top, orchard and June grass were still negative.

It is generally known that hay-fever may develop in persons who have had asthma due to other causes for some time. In this type of case it is assumed that the pollen sensitization has been existent for some time prior to the actual onset of hay-fever symptoms. However, there is no report in the literature of subjects in whom hay-fever and pollen skin tests were known to be negative, who subsequently develop clinical hay-fever, confirmed by positive cutaneous reactions first elicited at that time. The following two cases are of this character.

I have omitted everything in the past or present history that is not pertinent.

Case 1.—M. S., a boy, aged 4 years, had a history of onset of asthma five weeks before coming under observation on April 11, 1922. He was tested in a routine manner and showed positive reactions to the following: Rabbit hair, horse dander, duck and goose feathers, dog hair, orris root, lactalbumin, corn, rice, oat, barley, carrot, onion, radish, tomato and rhubarb. The etiologic sensitizations were rabbit hair, horse dander and feathers. After appropriate treatment, the child has been free from asthma for over three and one-half years. In June, 1924, rhinorrhea developed. Cutaneous tests with the pollen were repeated and for the first time reactions to the following were obtained: Timothy, +++; red-top, +; orchard grass, ±; June grass, ±, and ragweed short, +. No clinical

symptoms were observed during the ragweed season. However, it is interesting to note that the pollen seasons of 1925 were passed without any symptoms of hay-fever, although no treatment was given. In April of that year, this boy suffered from an afebrile scarlet fever.

CASE 2.—M. R., a boy, aged 5, with a history of onset of asthma at 2 years, first came under observation on Aug. 10, 1922. Routine protein skin tests revealed positive reactions to house dust, rabbit hair, horse dander, duck feathers, orris root, egg, lactalbumin and rhubarb. The etiologic sensitizations were horse dander and egg. After appropriate treatment, the patient remained free from all symptoms for seventeen months. In June and July, 1924, definite hay-fever symptoms without asthma were manifest for the first time, and on August 5, the patient was tested with the pollens and showed the following reactions: timothy, +; orchard and June grasses, ++. In 1925, preseasonal pollen therapy was commenced. The patient was entirely free from hay-fever until the first week in July, when he went to the country and experienced mild hay-fever symptoms only. At the time of writing, he had been free from asthma for over three years.

In summarizing the pollen sensitizations manifest in children, it may be definitely stated that a negative cutaneous test to pollen does not rule out such a sensitization. The conjunctival test with natural dry pollen is a simple, safe and dependable diagnostic method of eliciting sensitization in the presence of a positive history and negative cutaneous reactions, as evidenced by the cases cited in this study. It appears that pollen sensitization may be acquired, as evidenced by the two cases cited in the foregoing.

SENSITIZATION TO BACTERIAL PROTEIN

Walker [24] is credited with having first called attention to the possibility of "bacterial sensitization" in asthma. The publication of his extensive researches aroused widespread interest. The early literature on the subject seemed to be generally confirmatory. Later, confusion crept in, and now, many workers, including those who early published laudatory reports, have discarded it entirely. This seems to be a

24. Walker, I. C., and Adkinson, June: Study I. Studies in Staphylococcus Pyogenes Aureus, Albus and Citreus, and on Micrococcus Tetragenenus and M. Catarrhalis, J. M. Res. **35**:373 (Jan.) 1917; Study II. Studies on a Diphtheroid Organism Isolated from the Sputum of Patients with Bronchial Asthma, ibid. **35**:391 (Jan.) 1917. Walker, I. C.: Study III. Studies on the Sensitization of Patients with Bronchial Asthma to Bacterial Proteins as Demonstrated by the Skin Reaction and the Methods Employed in the Preparation of these Proteins, ibid. **35**:487 (Jan.) 1917; ibid. Study XII. Complement Fixation and Precipitin Reactions with the Serum of Bronchial Asthmatics Who Are Sensitive to the Proteins of Wheat, Horse Dandruff, Cat Hair, and Bacteria, Using these Proteins as Antigens, and the Cutaneous Reaction as an Index of Sensitization, ibid. **36**:243 (May) 1917. Walker, I. C., and Adkinson, June: Study XIII. The Relationship Between the Cutaneous Reaction, Serum Agglutination Tests and Bacteriological Examination of the Sputum and Nasal Secretions in Determining the Part Staphylococcus Pyogenes and Albus May Play In the Cause of Bronchial Asthma, ibid. **36**:295 (May) 1917. Walker, I. C.: Study XIV. The Treatment of Patients with Bronchial Asthma with Subcutaneous Injections of the Proteins to which They Are Sensitive, ibid. **36**:423 (July) 1917.

reaction from the excessive enthusiasm with which Walker's work was at first received. To discard this phase of the asthma question is a mistake. Calmer observations will no doubt give it its proper place in this field.

There are two methods of testing with bacterial proteins, namely, the scratch method, as first recommended by Walker, and the intradermic with the standardized vaccine containing the whole bacterial body, as recommended by Rackermann [25] and by Thomas and Touart.[26] Neither of these methods have proved satisfactory. The scratch method is unsatisfactory because the bacterial protein is of such small potency and the skin reactions they produce are so few that they give very little definite information. The intradermic method is equally unreliable because the skin reactions produced are very often of a nonspecific irritant character. With both methods the checking up of the skin reaction rarely coincides with the clinical aspect of a case.

The vast amount of clinical evidence at hand would indicate that the fault lies in the method of preparation of the bacterial protein extracts. For it cannot be denied that bacterial infection (which precedes bacterial sensitization in the opinion of many authors), particularly of the bronchial mucous membrane and upper respiratory tract, plays an important rôle in many subjects with asthma—protein and nonprotein sensitive. The whole question of bacterial protein sensitization and its relation to infection in asthma is indeed a complex problem, and has not as yet been solved by the methods of skin testing employed at present.

In recent years, a great deal of attention has been focused on bacterial allergy in animals.

Sherwood and Stoland,[27] studying typhoid protein sensitization in guinea-pigs, have confirmed their former conclusions [28] that the Dale reaction is not a necessary criterion of bacterial sensitization. They have shown that, in focally infected guinea-pigs, the skin reaction can be obtained from eight to thirteen days after infection, at which time the uterine horns show greater tolerance (for typhoid proteins) rather than specific reactions. Also "that in bacterial anaphylaxis, carefully

25. Rackermann, F. M.: Relation of Sputum Bacteria to Asthma, J. Immunol. **5**:373 (July) 1920.

26. Thomas, W. S., and Touart, M. De M.: Treatment of Asthma with Autogenous Vaccines, Arch. Int. Med. **34**:79 (July) 1924. Thomas, W. S., Famulener, L. W., and Touart, M. De M.: Autogenous Vaccines in Diagnosis, with Special Reference to Asthma, ibid. **34**:85 (July) 1924.

27. Sherwood, N. P., and Stoland, O. O.: Further Studies on Bacterial Anaphylaxis, J. Immunol. **10**:643 (July) 1925.

28. Sherwood, N. P., and Stoland, O. O.: Proceedings of the Society of American Bacteriologists. Abstr. J. Bacteriol. **5**:18, 1921; Bacterial Anaphylaxis, J. Immunol. **8**:141 (March) 1923.

controlled clinical criteria with profound shock and death as an end-point, yielded more positive results than the smooth muscle reaction of Dale."

Experimental studies have been carried out by Zinsser and his co-workers for a number of years; with Parker [29] in 1917, he experimented on the sensitization of guinea-pigs with typhoid bacilli. In 1921, Zinsser [30] succinctly stated that "it has been quite apparent to all workers in bacterial anaphylaxis that the sensitization of animals to the cell materials of the bacteria is much more difficult than is analogous sensitization with sera, egg, albumin, etc., and it has usually been assumed, and we believe correctly, that this was due to the relatively small amount of coagulable protein in the bacterial cell."

In 1923, Zinsser and Parker [31] studied staphylococci and typhoid bacilli, and in the following year Zinsser and Mallory [32] reported on pneumococcus allergy. In 1925, Zinsser and Grinnel [33] reported the allergic reactions to hemolytic streptococci, and were of the opinion that all bacterial allergies were based on identical fundamental phenomena, one of which was that sensitization was most successful when the whole bacteria was injected, in contrast to the less uniform and less intense effects when morphologically and chemically changed bacterial products were employed. It is of interest to note that the most potent material for demonstration of skin reactions in streptococcus allergy in guinea-pigs was the broth filtrate of streptococcus cultures.

Finally, Zinsser and his co-workers [34] plausibly states that the "fundamental biologic significance of bacterial allergy is an increased specific adjustment of the tissue for response to the stimulus of infection, and a consequently enhanced capacity for the rapid mobilization of the protective mechanism. When this mechanism is called into play against a qualitatively and quantitatively slight invasive assault, infection or superinfection may be slowed down or prevented." This same increased reaction capacity may become injurious or even fatal if called into play to an excessive degree in the course of an infection.

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29. Zinsser, H., and Parker, J. T.: Studies on Bacterial Anaphylaxis and Infection, J. Exper. Med. **26**:411 (Sept.) 1917.

30. Zinsser, H.: Studies on the Tuberculin Reaction and on Specific Hypersensitiveness in Bacterial Infection, J. Exper. Med. **34**:495 (Nov.) 1921.

31. Zinsser, H., and Parker, J. T.: Bacterial Hypersusceptibility, J. Exper. Med. **37**:275 (Feb.) 1923.

32. Zinsser, H., and Mallory, J. B.: Observations on Bacterial Anaphylaxis with Pneumococcus, J. Immunol. **9**:75 (March) 1924.

33. Zinsser, H., and Grinnell, F. B.: Further Studies on Bacterial Allergy. Allergic Reaction to the Hemolytic Streptococcus, J. Immunol. **10**:725 (June) 1925.

34. Zinsser, H.; Ward, H. K., and Jennings, F. B.: The Significance of Bacterial Allergy as a Sign of Resistance, J. Immunol. **10**:719 (June) 1925.

With the experimental data already at hand, the future for this phase of the subject appears exceedingly hopeful.

After all, the only clue on which the diagnosis of the possibility of a specific bacterial sensitization in a subject can only be based on the information derived from a detailed history and repeated clinical observations of the course and effect of infections on the asthmatic state. Thus, after a case is thoroughly investigated and all other causal factors eliminated, then purely from a clinical point of view one can reasonably assume that he is dealing with bacterial asthma (now classified under the nonallergic group for obvious reasons).

Bacterial infection superimposed on a protein sensitive asthma is similarly recognized from a purely clinical basis.

In this series, twelve stock bacterial proteins, prepared after the method of Walker, were employed as a routine. Bacterial protein sensitization (with the material and method used) in these children was uncommon. Two patients gave plus-minus reactions to *Staphylococcus pyogenes-aureus* and *Bacillus coli*. Four other patients gave delayed skin reactions as follows: three to *Streptococcus hemolyticus* and one to Friedländer's bacillus, *Bacillus coli* and *Micrococcus catarrhalis*. In the latter patient the bacterial protein skin reactions proved to be an aid in determining one of the etiologic factors in asthma.

SENSITIZATION TO FOOD PROTEINS

A decade has passed since Talbot [35] stated that "during infancy and childhood, practically all cases of sensitization are due to food." This statement was generally accepted and seemed to be verified by the limited number of cutaneous tests then employed, because attention was focused almost entirely on food allergy at that time. Today, while it is still evident that food sensitization plays a more important rôle in children than in adults, yet it is secondary in importance to the part played by the inhalant group in the causation of asthma. In this series, every patient exhibiting cutaneous reactions to food proteins also reacted positively to one or more of the inhalants, while the reverse was not true.

Since nearly all the children of this series were Jewish, having dietary customs and habits peculiar to the tenets of their faith, comparisons of my findings with the statistical reports of other authors of mixed nationalities and different classes would serve no purpose.

The total number of positive food reactions, and the number of patients reacting in relation to the age of onset of asthma, are shown in chart 8.

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35. Talbot, F. B.: Idiosyncrasy to Cow's Milk. Its Relation to Anaphylaxis, Boston M. & S. J. **175**:409 (Sept. 21) 1916; Relation of Food Idiosyncrasies to Diseases of Childhood, ibid. **179**:285 (May 29) 1918.

Seventy-one per cent of the protein sensitive group and 56 per cent of the entire series accounted for the 274 positive food reactions charted. Of these, 127 were plus and 147 were plus-minus reactions. Twenty-nine, or approximately one-half of these patients, gave no food reactions larger than a plus-minus reaction. It is of interest to note that a greater number of plus-minus than plus reactions was recorded. As with the inhalant group, it will be seen that the number of patients reacting to the food proteins reaches the peak with the age of onset at 2 years.

It is apparent from a study of chart 8 that of the fifty-six patients showing a total of 274 food reactions, 260 occurred in fifty between

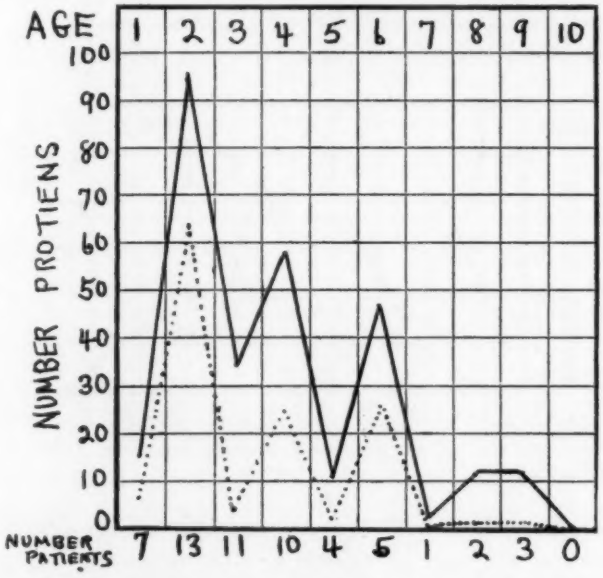

Chart 8.—The total number of positive food reactions and the number of patients reacting in relation to the age of onset of asthma. Plain line, total positive food reactions. Broken line, one to four plus reactions only.

the ages of 1 and 6 years inclusive. Thus, 94 per cent of the total number of food reactions occurred in 89 per cent of the patients with onset of asthma from 1 to 6 years, inclusive, which would indicate that food sensitization in children with asthma mostly takes place prior to the seventh year, at least in this series.

There was an average of five reactions per patient. The average number of food reactions per patient in relation to the age of onset is shown in chart 9. The largest number of reactions per patient occurred in those with the age of onset between 2 and 6 years, inclusive. It is significant that the largest number of positive reactions per patient

occurred with the onset at 2 and 6 years, 7 and 9 food reactions per patient, respectively. The peak occurring at 6 years is only relative, because most of these patients were found to react to entire food groups such as the meats and fishes, which accounted for the greatest number of food reactions per patient occurring at this age.

The total number of positive food reactions and the number of patients reacting with relation to the age when the patients were first tested, are shown in chart 10. The average number of food reactions per patient are shown in chart 11. The usefulness of these food charts is obvious, yet the real value only becomes enhanced when a comparative study is made from a similar chart (chart 6) involving the inhalant sensitizations. It appears from the comparison of the charts (charts 6 and 11) that the number of inhalant reactions per patient is about evenly distributed throughout all ages, and that the average number of

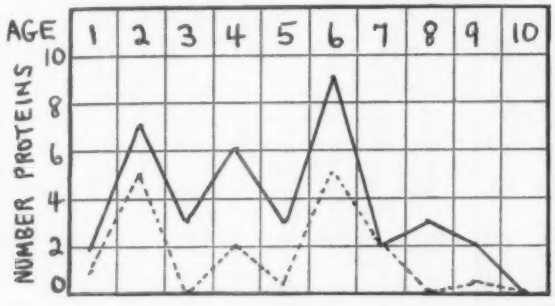

Chart 9.—The average number of food reactions per patient in relation to the age of onset of asthma. Plain line, total positive reactions. Broken line, one to four plus reactions only.

reactions is four; whereas the greatest number of food reactions per patient occurs at the ages of 6 and 8, after which the curve sharply declines and maintains a low level for the remaining ages. The peak at 3 years is abnormal because it represents only one patient who happened to have exhibited a multiple hypersensitivity. Between the ages of 3 and 8 years, inclusive, there was an approximate average of seven food reactions per patient as compared to 3.86 inhalant reactions. Between the ages of 9 and 14 years, inclusive, the approximate average number of reactions was 3 for the foods and 4 for the inhalants. In other words, children tested for the first time to inhalants show that the average number of reactions per patient is found to be about the same for all ages, and the children so tested for food proteins begin to show the phenomenon of natural desensitization after the eighth year. Natural desensitization to the inhalants, however, does not seem to occur.

It is impractical, if not almost impossible, to determine the exact rôle in the etiology of every food to which a patient reacts. A repeated his-

tory of allergic symptoms following the ingestion of certain foods, together with a positive skin reaction, are undisputed evidences of cause and effect. A patient may exhibit symptoms from the ingestion of only one or two of the many foods to which he shows positive skin reactions, while another patient may ingest any one of the foods to which he is sensitive without inducing symptoms; but if more than one of these foods or an unusual quantity of one food is ingested, then allergic

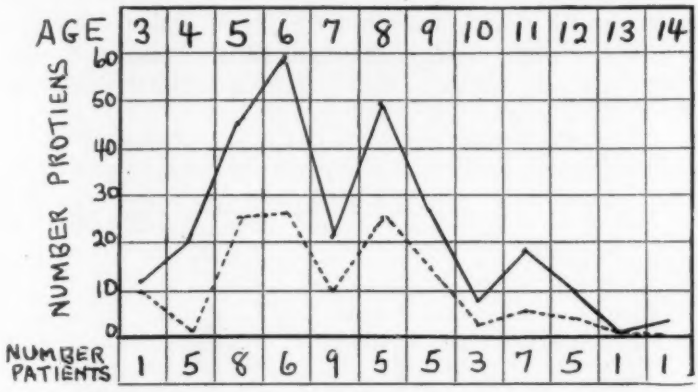

Chart 10.—The total number of positive food reactions and the number of patients reacting in relation to tne age when first seen. Plain line, total positive reactions. Broken line, one to four plus reactions only.

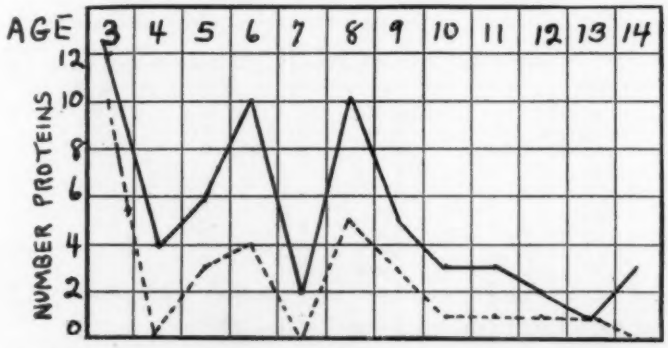

Chart 11.—The average number of food reactions per patient in relation to the age when first seen. Plain line, total positive reactions. Broken line, one to four plus reactions only. The number of proteins per patient at the age of 3 is not representative for that age, since it accounts for only one multiple hypersensitive case.

symptoms become manifest. It may be reiterated that all patients exhibiting food sensitiveness also react to one or more inhalant substances. Thus, it often happens that a patient will be unable to tolerate a food to which he is sensitive while exposed to the concurrent inhalants, but on the removal of the inhalant substance the same food may be

readily tolerated. For these and for other reasons, tables summarizing etiologic food sensitizations are speculative at their best, and are therefore purposely omitted.

Tables 11 to 18, inclusive, show the various proteins to which the patients gave positive reactions, arranged in food groups. Only those patients who gave positive reactions are recorded.

Of the thirty patients sensitive to one or more of the cereals (table 11), eight reacted to wheat or to one, or more, of its split proteins, in conjunction with one, or more, cereal grains. Two patients reacted to whole wheat only, while seven patients reacted to only one, or more, of the split wheat proteins. Eleven patients reacted to one,

TABLE 11.—*Sensitization to the Cereal Grains*

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Wheat (whole)	6	0	6	7.60	6.00
Wheat glutenin	1	0	1	1.20	1.00
Wheat globulin	11	2	13	16.40	13.00
Wheat leucosin	1	2	3	3.70	3.00
Wheat proteose	2	2	4	5.00	4.00
Barley	4	7	11	13.90	11.00
Buckwheat	1	0	1	1.20	1.00
Corn	3	0	3	3.70	3.00
Oat	2	1	3	3.70	3.00
Rice	6	1	7	8.80	8.00
Rye	4	1	5	6.30	5.00

TABLE 12.—*Sensitization to Egg and Milk*

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Egg, whole	5	4	9	11.50	9.00
Egg white	1	6	7	8.80	7.00
Egg yolk	1	5	6	7.60	6.00
Milk, cow's	2	1	3	3.70	3.00
Casein	1	0	1	1.20	1.00
Lactalbumin	6	2	8	10.10	8.00
Cheese	4	0	4	5.00	4.00

or more, of the cereal grains not in conjunction with wheat or its split proteins. One patient reacted to buckwheat alone.

Wheat globulin is the most frequent cereal grain protein reaction met with, comprising 16.4 per cent of the protein sensitive group or 13 per cent of the entire series. Next in order of frequency are: barley, rice, rye, oat, corn and buckwheat.

Of the nine patients sensitive to eggs (table 12), six reacted to all of the egg protein extracts, one to whole egg and egg white, and two to whole egg but not to either of its split proteins. They were both plus-minus reactions.

Of the ten patients reacting to milk and its constituent proteins, one reacted to milk, casein, lactalbumin and cheese; two to milk and

lactalbumin; one to lactalbumin and cheese; four to lactalbumin alone, and two to cheese alone.

Lactalbumin is the most important constituent of milk, and casein the least important.

Of the ten patients sensitive to the various meats (table 13), two reacted to all meat proteins; one to all but goose meat; two reacted to beef alone. Two reacted to goose alone and one each to chicken, veal and lamb. The incidence of sensitization is about the same for all of the proteins.

TABLE 13.—*Sensitization to Meats*

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Beef	2	3	5	6.30	5.00
Chicken	3	1	4	5.00	4.00
Goose	2	2	4	5.00	4.00
Lamb	3	1	4	5.00	4.00
Veal	2	2	4	5.00	4.00

TABLE 14.—*Sensitization to Fish* *

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Herring	1	5	6	7.60	6.00
Mackerel	0	4	4	5.00	4.00
Pike	2	6	8	10.10	8.00
Salmon	0	6	6	7.60	6.00
Smelts	0	6	6	7.60	6.00

* Other fish proteins and the shell fish are not listed here because they were not employed in routine testing.

TABLE 15.—*Sensitization to Vegetables*

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Asparagus	2	0	2	2.50	2.00
Beans	1	0	1	1.20	1.00
Beet	0	2	2	2.50	2.00
Cabbage	1	1	2	2.50	2.00
Carrot	2	0	2	2.50	2.00
Cucumber	6	3	9	11.30	9.00
Lentil	0	1	1	1.20	1.00
Lettuce	7	3	10	12.60	10.00
Lima beans	0	1	1	1.20	1.00
Mustard *	2	5	7	8.80	7.00
Onion	1	0	1	1.20	1.00
Pea	1	1	2	2.50	2.00
Potato	1	5	6	7.60	6.00
Radish	9	8	17	21.50	17.00
Rhubarb	2	1	3	3.70	3.00
Tomato	2	2	4	5.00	4.00

* Mustard is included here because it is used orally, but in children it acts essentially as an inhalant.

Nine patients reacted to fish (table 14). Four of these patients reacted to the entire fish group; two to all, with one exception, herring and mackerel respectively. Of the remaining three patients, one reacted to herring alone and two to pike alone. These accounted for the only plus-minus sensitizations.

Thirty-four patients reacted to one or more vegetable proteins (table 15) fifteen of these patients reacted to only one vegetable protein; one each to pea, rhubarb, carrot and tomato; two each to potato; two each to cucumber; three each to radish and four each to lettuce.

Eleven patients reacted to two vegetable proteins; one to asparagus and cucumber; one to beet and tomato; one to cucumber and radish; one to radish and rhubarb; one to tomato and radish; two to cucumber and lettuce, and four to mustard and radish.

Four patients reacted to three vegetable proteins; one to radish, lettuce and tomato; one to potato, radish and mustard; and two to radish, lettuce and cucumber.

Two patients reacted to four vegetable proteins; one to radish, mustard, beet and lima bean; and the other to radish, lettuce, cucumber and potato.

TABLE 16.—*Sensitization to Nuts*

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Almond	3	2	5	6.30	5.00
Brazil nut	2	5	7	8.80	7.00
Chestnut	2	1	3	3.70	3.00
Peanut	1	0	1	1.20	1.00
Walnut	2	0	2	2.50	2.00

TABLE 17.—*Sensitization to Fruits*

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Canteloup	1	0	1	1.20	1.00
Fig	1	0	1	1.20	1.00
Orange	1	0	1	1.20	1.00
Pear	2	0	2	2.50	2.00
Pineapple	1	1	2	2.50	2.00
Strawberry	3	0	3	3.70	3.00

One patient reacted to five; carrot, onion, radish, rhubarb and tomato, and one reacted to eight; asparagus, bean, lentil, mustard, pea, potato, radish and tomato.

Twenty-seven of the thirty-four patients reacted only to one or two vegetables. It is significant that the seven mustard sensitizations occurred always in conjunction with radish, and that radish and mustard together occurred as the only sensitization in four patients.

Thirteen patients reacted to nut proteins (table 16). Eight reacted to only one nut protein; five to brazil nut; two to almond and one to chestnut.

Four patients reacted to two proteins; two to brazil nut and almond; one each to chestnut and almond, and chestnut and walnut. One patient reacted to three: chestnut, peanut and walnut.

Ten patients reacted to fruit proteins (table 17). No patient reacted to more than one fruit.

Eighteen patients reacted to the beverages (table 18). None reacted to more than one beverage.

Table 19 is a summary of the incidence of positive food reactions in this series. Proteins involving less than 3 per cent of the total are omitted.

COMMENT ON SENSITIZATION TO FOOD PROTEINS

The significance and fate of the food reactions are better understood when studied in relation to the onset of asthma and the age when first tested.

In this series, there were cases of food intolerance commencing in early childhood, in which the history pointed to an undoubted food

TABLE 18.—*Sensitization to Beverages*

Protein	Number Reactions			Percentage Protein Sensitive Group	Percentage Entire Series
	±	+	Total		
Coffee	12	3	15	18.90	15.00
Cocoa	1	1	2	2.50	2.00
Tea	1	0	1	1.20	1.00

TABLE 19.—*Summary of Cutaneous Sensitization to Food Proteins* *

Protein	Percentage Protein Sensitive Group	Percentage Entire Series	Protein	Percentage Protein Sensitive Group	Percentage Entire Series
Radish	21.50	17.00	Almond	6.30	5.00
Coffee	18.90	15.00	Beef	6.30	5.00
Wheat globulin	16.40	13.00	Rye	6.30	5.00
Barley	13.90	11.00	Cheese	5.00	4.00
Lettuce	12.60	10.00	Chicken	5.00	4.00
Egg, whole	11.30	9.00	Goose	5.00	4.00
Cucumber	11.30	9.00	Lamb	5.00	4.00
Pike	10.10	8.00	Mackerel	5.00	4.00
Lactalbumin	10.10	8.00	Tomato	5.00	4.00
Egg white	8.80	7.00	Veal	5.00	4.00
Brazil nut	8.80	7.00	Wheat proteose	5.00	4.00
Mustard	8.80	7.00	Chestnut	3.70	3.00
Rice	8.80	7.00	Corn	3.70	3.00
Egg yolk	7.60	6.00	Oat	3.70	3.00
Herring	7.60	6.00	Milk (whole)	3.70	3.00
Salmon	7.60	6.00	Rhubarb	3.70	3.00
Smelts	7.60	6.00	Strawberry	3.70	3.00
Potato	7.60	6.00	Wheat leucosin	3.70	3.00
Whole wheat	7.60	6.00			

* Includes only foods giving an incidence of more than 3 per cent.

sensitization (wheat, milk and eggs). When these patients were first tested by me, negative reactions as well as a history of an acquired tolerance to these foods were obtained. In the few subjects still showing positive skin reactions, complete tolerance to these foods were demonstrated under varied conditions; still the asthma persisted, and some other acquired sensitization, usually an inhalant, was responsible for the symptoms.

In a third group of children, positive food reactions were elicited when they first came under observation. These foods proved to be partially responsible for the presenting symptoms. These sensitizations,

however, disappeared after a total abstinence of these foods from the diet of the children for a period of from six months to two years. This was evidenced by repeated negative cutaneous reactions. After these periods of abstention, symptoms no longer followed ingestion of these foods. There is another small group of children usually sensitive to fish, meats and nuts, whose intolerance for these foods could not be controlled even by abstinence for long periods. These particular foods seem to have a tendency to sensitize, of a power and persistency equal to that of the inhalant group of proteins. In this group of children, there is usually a history of eczema during infancy.

It has been observed that in patients with multiple food sensitization that they can ingest several of these foods in moderate amounts, and fairly frequently without inducing symptoms. Under similar conditions, when the patients ingest an unusual quantity of these foods, then symptoms develop. Again, patients may be able to tolerate one of these foods in reasonable amounts without symptoms, while more than one will produce symptoms. This observation suggests that the sum of several mild food sensitizations will cross the threshold of maximum tolerance and induce symptoms. From a clinical point of view, the dietetic treatment of such cases is suggestive.

Certain foods or food groups induce eczema, urticaria or angioneurotic edema, while other foods cause asthma in the same patient. In this connection it may be stated that approximately one-half of the etiologic egg and fish sensitizations encountered in these asthmatic children were responsible for only cutaneous and digestive manifestations of allergy. In other cases, it was found that ingestion of various foods was responsible for intestinal cramps or for a persistent cough. This fact was clearly demonstrated in a patient with asthma, in whom rabbit hair was the sole etiologic factor, while the ingestion of herring was definitely responsible for what clinically appeared to be "bronchitis." The restriction of herring from the diet promptly cleared up the "bronchitis," and the skin reaction in this subject became negative after one year of total abstinence from herring. At the end of this time, this food was ingested without causing any symptoms.

Certain food proteins in biologic groups, such as meats and fishes as a whole, proved to be of definite clinical significance in the dermatoses. These observations will form the subject of a future publication.[36]

Radish, coffee, wheat globulin, barley, lettuce, etc. (table 19) are the most common positive food reactions encountered in these children, yet foods such as egg, fish and nut are directly responsible for most of the symptoms attributed to food intolerance. Milk usually causes trouble

36. Peshkin, M. M.: Studies on Asthma in Children. II. The Incidence and Significance of Eczema, Urticaria and Angioneurotic Edema (to be published).

in late infancy and early childhood, and by the time these children come to the clinic, the tolerance to milk has been fully acquired, often in spite of a positive skin reaction to lactalbumin which was the constant offender.

The occurrence of radish and mustard as the only vegetable sensitizations in 5 per cent of the protein sensitive group is of special interest, in view of the fact that these foods were not ingested. The mustard sensitization can be attributed to the application of it as a plaster applied to the chest for the relief of an attack of asthma. Subsequently, the use of mustard plasters were observed to exaggerate the attack of asthma. The frequent association of radish and mustard sensitizations would indicate that these two foods have something in common.

The size of the cutaneous reaction does not necessarily indicate the degree of sensitiveness or the tolerance of the patient to the reacting food. It cannot be too strongly emphasized that the plus-minus reactions should be regarded as definitely positive. Clinically, the proper interpretation of these small reactions often led to important information. I have seen patients with multiple plus and plus-minus reactions against different proteins who were markedly improved or recovered when one or all of the latter were seriously considered as etiologic factors.

SENSITIZATION TO HORSE SERUM

Five patients, or 6 per cent of the protein sensitive group, showed positive skin reactions to horse serum. Only one of these showed direct contact with horse serum by a prophylactic injection of diphtheria antitoxin one and one-half years before the onset of asthma. Three of these patients reacted to horse dander, in one of whom horse dander was an etiologic sensitization.

Peshkin and Rost [2] determined the incidence of sensitization to horse serum in 477 normal children. Only one of their series gave a plus-minus reaction to horse serum. This child had a negative history to diphtheria, and had never been injected with any kind of serum. Thus the incidence of horse serum sensitization was 0.2 per cent in normal children, as compared to 6 per cent in the asthmatic children sensitive to protein.

In regard to this series, only one child showing a reaction to horse serum was injected prior to the onset of asthma, after which he was first tested. This injection of horse serum was not followed by deleterious effect. However, it is impossible to determine if this child was sensitive to serum before his inoculation. It is just as possible that the inoculation sensitized him. The other four showing an inherent sensitization were never inoculated with horse serum. Deaths following the administration of therapeutic animal serums have been reported in

the literature. It is highly probable that these unfortunate subjects were inherently sensitive to serum. With the growth in popularity of the application of therapeutic serums, it is more important than ever not to relax our efforts to search for a possible sensitization in every patient about to be injected.

SENSITIZATION TO DRUGS

Protein skin sensitizations have been reported to ipecac, rhubarb and lycopodium by me,[37] to ipecac by Widal and his co-workers,[38] and to castor bean by Bernton.[39] Allergic symptoms followed contact with, and inhalation of, these drugs.

Asthma following ingestion of various other drugs has been frequently observed, especially to acetyl-salicylic acid, since this drug came into such general use. All these sensitizations were in adults.

None of the children of this series nor in my experience has shown any drug intolerance.

POSITIVE PROTEIN SKIN REACTIONS BEARING NO RELATION TO THE ETIOLOGY OF ASTHMA

It is a fairly common experience of workers engaged in the study of asthma to find patients with positive skin reactions to various proteins, but in whom these reactions could not in any way be harmonized with the previous or present history.

That a condition of this sort is more readily demonstrable in children than in adults is obvious. Certain definite criteria, however, had to be complied with before a case could be considered as belonging to this group. The children were observed through all seasons of the year. The effect of exposure to the reacting proteins, of diet, of environment, as well as response to indicated treatment were carefully noted. If the history of any one of these subjects pointed to the least suggestion of protein intolerance, in such, the condition was considered allergic asthma, in spite of the many nonspecific factors responsible for the continued asthma, and was, accordingly, excluded from this group.

Ten patients, or 12 per cent of the protein sensitive group, belong to this group. These patients showed a total of 30 positive reactions, ranging from 1 to 8 per patient. The average number of reactions was three and three-quarters per patient. The reactions occurred in their order of frequency, as follows: house dust, 6; duck feathers, 4;

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37. Peshkin, M. M.: Ipecac Sensitization and Bronchial Asthma, J. A. M. A. **75**:1133 (Oct. 23) 1920; Bronchial Asthma and Other Allergic Manifestations in Pharmacists, ibid. **82**:1854 (June 7) 1924.

38. Widal, F.; Abrami, P., and Joltrain, E.: Anaphylaxis to Ipecac, Presse méd. **30**:341 (April 22) 1922.

39. Bernton, H. S.: Occupational Sensitization to the Castor Bean, Am. J. M. Sc. **165**:196 (Feb.) 1923.

radish, 3; mustard, 2; barley, 2; orchard grass (c), 2; June grass (c), 2; and orris root, rabbit, camel and goat hair, fig, wheat globulin, ragweed (c), timothy (c) and red-top (c), 1 each. Recalling what has already been said of house dust, it is interesting to note that dust is the most common of the reactions occurring in this group. In the foregoing, c refers to conjunctival reaction.

Of these ten children, three gave a history of onset of asthma following pneumonia, and one following pertussis; in these subjects, attacks of asthma were always associated with upper respiratory infections; three had chronic bronchitis and emphysema with a history of recurrent upper respiratory infections, and three always had asthma several days after contracting definite acute rhinitis, often acquired from other members of the household. These patients, with the exception of one, were free from asthma, for the most part, during the warmer months of the year.

How then can one account for these cutaneous reactions? It is obvious that they cannot be regarded as nonspecific or irritative reactions. There is always the possibility that in this group the sensitizing substance responsible for the asthma may not have been detected; but everything was done in our present knowledge to work the cases up thoroughly, both as to diagnosis and treatment, without results. In addition to the routine tests, search for unusual sensitizations were made without avail. My position is justified that this group is of some significance and should be clinically recognized, particularly since 10 per cent of normal children [2] show positive reactions to various proteins.

For these reasons, although these subjects had positive skin reactions, they were kept in a group separate from those with true allergic asthma, and from the point of view of treatment were considered in the same light as the group with nonprotein sensitive asthma.

THE INFLUENCE OF NONSPECIFIC FACTORS IN ASTHMA

The influence, directly or indirectly, of various diseases and infections of childhood, of tonsillectomies, adenoidectomies [40] and the family history,[41] on asthma were studied in detail and will be the subjects of future communications.

(B) NONPROTEIN SENSITIVE ASTHMA

Eighteen patients, or 18 per cent of this series, make up the nonprotein sensitive group. The age of onset of asthma ranged from 8 months to 8½ years, and is fairly evenly distributed except around the

40. Peshkin, M. M.: Studies on Asthma in Children. III. The Incidence and Significance of Various Diseases and Infections, and of Tonsillectomy and Adenoidectomy (to be published).

41. Peshkin, M. M.: Studies on Asthma in Children. IV. The Family History (to be published).

age of 1 year when the condition occurred in five. The average age of onset per patient was 4.22 years. The average age of onset in the protein sensitive series was 3.9 years. The age when the patients were first seen ranged from 1 to 14 years. The average was 7.2 years, while in the protein sensitive group the average was 8.04 years per patient.

Six patients gave a history of onset of asthma following pneumonia; two of these have a chronic unresolved pneumonia, and one of these also has a cylindric type of bronchiectasis.

Nine patients gave a history of repeated upper respiratory infections contracted in the autumn and winter, from eight months to two years prior to the onset of asthma. Two patients had asthma following pertussis.

One patient had asthma as a result of a focal infection—left chronic suppurative otitis media. Whenever the oral discharge was checked by medical treatment, asthmatic attacks would occur, which were followed by relief only when pus drained freely again. A pure culture of *Staphylococcus pyogenes-albus* was isolated the first time and a year later *Streptococcus anhemolyticus;* vaccines of each at those times were used, with complete relief to the patient.

All of these patients had varying degrees of chronic bronchitis, and four of them had chronic emphysema with resulting chest deformity.

(C) PARA-ASTHMA

Among the nonprotein sensitive cases there is a group which clinically cannot be distinguished from other types of asthma. From the point of view of etiology and the pathologic conditions found in these children which have a direct bearing on the etiology, they must be differentiated from all other groups. These cases are directly caused by either an enlarged thymus or enlarged bronchial lymph nodes, or both. They are sometimes referred to as obstructive asthma. This is an inadequate term, since many subjects with these abnormalities do not show asthmatic symptoms. I have called this group "para-asthma," a term which, though not descriptive of the type, is at least not misleading.

The age of onset of asthmatic symptoms in para-asthma is significant. It invariably occurs within the first 18 months of life. There were three cases, or 3 per cent, of para-asthma in this series. I am citing the pertinent findings of these three cases as the best method of presenting the characteristics of para-asthma.

REPORT OF CASES

CASE 1.—E. A., a boy, aged 7½ months, gave a history of gradual onset of asthmatic symptoms, which came and went since the age of 1 month. Roentgenoscopy of the chest confirmed the presence of an enlarged thymus. The Pirquet reaction was negative.

CASE 2.—A. K., a boy, aged 20 months, gave a history of gradual onset of asthmatic symptoms commencing at 1 year, always associated with upper respiratory infections, with only brief periods of relief from symptoms. Examination of the chest revealed the usual signs of asthma. The Pirquet reaction was negative. The intradermic test was positive with 2 mg. of tuberculin. Roentgenoscopy of the chest revealed a marked enlargement of the bronchial lymph nodes on both sides, forming fairly large tumor masses. This condition is not to be confused with "expiratory dyspnea," as described by Schick.[42]

CASE 3.—L. S., a boy, aged 18 months, gave a history of sudden onset of asthma following a tonsillectomy at 17 months. Examination revealed a typical asthmatic chest and an area of dulness extending to the left of the sternum. Roentgen-ray examination of the chest revealed an enlarged thymus and markedly enlarged bronchial lymph nodes. The Pirquet reaction was positive.

The condition in these three children was of extreme interest, because it was clinically recognized as asthma, and the subjects were referred to the clinic for treatment. In case 3, the condition was especially interesting, because it combined both thymus and glandular pathology.

Roentgen-ray therapy relieved these subjects of all their symptoms, and also improved the existing tuberculous condition. Roentgenograms showing the progress made at various stages of the treatment will be found in a future publication.[43]

COMMENT

This series, although comprising 100 cases, is interesting in that every one of the children was under observation for at least one year, the average observation per patient being two and one-third years. To keep this series under control, a great deal of energy was expended by the Social Service Department of Mount Sinai Hospital. For a detailed study of this character, 100 cases were considered sufficient. A larger series might have been used as well as a longer period of observation, but, due to the difficulties of control, it would only have resulted in a study of a series of selected cases. This study of 100 consecutive and controlled cases afforded better material from which to draw definite conclusions.

The clinical significance of the protein skin reactions is far from a closed chapter. After all, they are only of value when they lead to direct clinical results. There are many workers who consider the present status of the question as eminently satisfactory, and almost a complete science. Then again, there are far too many others, clinicians of repute, who still view the entire subject with skepticism. The existence of too many discrepancies in the interpretation of the reactions has lead to

42. Schick, B.: Expiratoresches Keuchen als Symptomatologie im Ersten Lebensjahre, Wien. klin. Wchnschr. **23**:153 (Feb. 3) 1910.

43. Peshkin, M. M.: Studies on Asthma in Children. V. Roentgenoscopy of the Chest and the Tuberculin Skin Reaction (to be published).

more or less indifferent results, and is largely responsible for the controversial situation. In this, and in subsequent studies on asthma in children, every effort has been made by detailed observation to secure a rational clinical conception of the rôle that these protein skin reactions actually play in the direct and contributory etiology of asthma.

It must be borne in mind that the various etiologic protein sensitizations are merely exciting factors and not the basic cause of asthma. What disturbed mechanism is primarily responsible for the varied manifestations of allergy in the human being is still unknown. Until such a mechanism is brought to light, we must content ourselves with the present method of eliciting the various exciting factors in asthma. Therefore, to fix the responsibility in asthma requires a complete series of protein skin tests accurately performed and properly interpreted, together with a thorough history, physical examination and careful study of the case, extending over a considerable period of time.

CONCLUSIONS

1. One hundred consecutive cases of asthma in children were tested in a routine manner with ninety-seven food, epidermal, pollen, bacterial and dust proteins by the cutaneous scratch method, and were observed for a period from one to four years; the average being two and one-third years.

2. The futility of employing inactive substances for the skin tests cannot be overemphasized.

3. All reactions above the control are definite positive reactions (scratch test). The importance of the plus-minus reactions have been clinically demonstrated.

4. A constitutional reaction following a scratch test has not occurred in this series, nor ever in my experience.

5. Asthma has been divided into three main groups, with their frequency of occurrence as follows: protein sensitive, 79 per cent; nonprotein sensitive, 18 per cent, and para-asthma (a new term) 3 per cent.

6. The most common age of onset of asthma in the protein sensitive group was 2 years. Onset of asthma after 10 years did not occur. The most common onset in the nonprotein sensitive group is around 1 year (27 per cent), and after that it is fairly evenly distributed up to the ninth year, after which no cases occurred. The age of onset in the para-asthma group is before 18 months.

7. Ninety-eight per cent of the patients of the protein sensitive group reacted to the inhalants. The most common inhalants in their order of frequency were: rabbit hair, house dust, duck feathers, horse dander, cat hair and ragweed. Sensitization to rabbit hair occurred in 49 per

cent of all asthmatic children, or in 62 per cent of the protein sensitive group. Patients who exhibited a positive skin reaction to rabbit hair were classified into five groups, according to the rôle that this sensitization played in the etiology. The most common primary sources of exposure were from pillows and mattresses. It may be conceded that house dust is responsible for more skin reactions than any other substance, but as an etiologic factor in asthma it does not assume the importance of rabbit hair. Duck and goose feathers sensitizations are common, while chicken feather sensitization is relatively uncommon in this class of children. One-half of the children of the protein sensitive group react to horse dander. However, as an etiologic sensitization it accounts for only 10 per cent of these cases, and in no case was it the sole etiologic factor. Positive skin reactions to rabbit hair and horse dander in the same person occurred in 43 per cent of the patients of the protein sensitive group. However, as an etiologic factor, asthma occurred three times more frequently with rabbit hair than it did with horse dander in these patients. Sensitization to cat hair occurred in 24 per cent of the entire series, or in 31 per cent of the protein sensitive group. It was a frequent contributory etiologic sensitization only. Twenty-five per cent of the protein sensitive group gave positive skin or conjunctival pollen reactions. Pollen was an etiologic factor in about half of these cases, and, of this, ragweed was the most common. One third of the cases with a pollen etiology were refractory to the cutaneous but positive to the conjunctival tests. Children with asthma having an etiologic pollen sensitization invariably showed other protein etiologic sensitizations. Two cases were cited in which a pollen history and the cutaneous reactions against pollen were negative when first tested. About two years later, both children acquired hay-fever, and then for the first time showed positive cutaneous reactions to pollens.

8. A reliable diagnosis of bacterial asthma cannot at present be made with materials obtainable and the methods employed.

9. Seventy-one per cent of the patients of the protein sensitive group gave positive food reactions. Food sensitization in asthmatic children usually takes place prior to the seventh year. The most common age of onset of asthma was 2 years. The phenomenon of natural desensitization generally occurs after the eighth year. Radish, coffee, wheat (globulin), barley and lettuce are the commonest food reactions encountered in these children, yet fish, egg and nut are directly responsible for most of the symptoms attributed to food intolerance. Cow's milk usually causes trouble in late infancy and early childhood. Mustard and radish sensitizations appear to have something biologically in common. Nine per cent of the protein sensitive cases, or one eighth of the cases giving food reactions, do so by reacting to entire food groups such as the fish

and meat groups or both. This is of diagnostic significance. Food plays an extremely variable rôle in the production of allergic symptoms in children, and does not attain the importance of the inhalant proteins.

10. Skin tests with horse serum should be performed in every case of bronchial asthma before the administration of therapeutic serums is attempted.

11. Drug intolerance has not been observed to occur in these children.

12. Positive protein skin reactions were found in 10 per cent of the children with asthma, in whom there was no etiologic connection. This is exactly the incidence of reaction occurring in normal children.

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TUBERCULOSIS OF ABDOMINAL LYMPH NODES

DIAGNOSIS BY MEANS OF THE ROENTGEN RAY *

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Tuberculosis of the mesenteric lymph nodes is found in children with great frequency, but the presence of the disease in these structures has been brought to light at necropsy or at operation rather than by examination during life. The pathologist often finds the lymph nodes of the abdomen the seat of caseous or calcifying tuberculosis, when the possibility had never entered the mind of the clinician, and the surgeon often encounters tuberculous nodes in the abdomen when fully expecting to meet an acute condition of a nontuberculous nature. In discussing abdominal tuberculosis in children, Still [1] points out that the condition is not common from the clinician's standpoint, "but from the more reliable estimate of the pathologist, abdominal tuberculosis would seem to be one of the commonest of all tuberculous lesions in children." "My own statistics," he writes, "show that 88.3 per cent of tuberculous children have tuberculous lesions in the abdomen." Though the diagnosis of infection with the tubercle bacillus can be made readily enough in the living subject by means of the intradermal tuberculin reaction, the site of infection often cannot be determined by any means.

REVIEW OF THE LITERATURE

In reviewing the literature on the diagnosis and symptomatology of tuberculosis of the abdominal lymph nodes, two points become apparent: first, the frequency with which tuberculous mesenteric lymphadenitis is confused with other conditions, and, second, the rarity with which it is diagnosed except at operation or at necropsy. Gehrels [2] pointed out that tuberculosis of the lymph nodes of the abdomen is frequently confused with surgical conditions, especially with appendicitis. Struthers [3]

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1. Still, G. F.: Common Disorders and Diseases of Childhood, Ed. 3, London, Henry Frowde, pp. 423 and 427, 1920.

2. Gehrels, E.: Die Mesenterialdrüsentuberkulose, Deutsche med. Wchnschr. **45**:1128-1130 (Oct. 9) 1919.

3. Struthers, J. W.: Mesenteric Lymphadenitis Simulating Appendicitis, Edinburgh M. J. **27**:22 (July) 1921.

reported four cases in which the diagnosis of appendicitis was made, but at operation tuberculous mesenteric lymphadenitis was found. Clute [4] directed attention to the difficulties in distinguishing calcified abdominal nodes from urinary stones, stating that the correct diagnosis may be impossible until pyelography is done. In a later paper,[5] he presented points in the differential diagnosis of the two conditions by means of the roentgenogram. The importance of taking a lateral view of the abdomen for differential diagnosis was brought out by Harvey in the discussion of Clute's paper. Valentin [6] discussed the subject of occlusion of the ureter by tuberculous mesenteric lymph nodes, and Fowler [7] reported a case of noncalculus cholecystitis in a young adult, the cause of which was a calcified lymph node lying in the cysticoduodenal ligament (an anomalous condition) proximal to the common bile duct. Mayo [8] and Ciaprini [9] each reported a case similar to that described by Fowler, and Ciaprini has summarized four more from the literature, all erroneously diagnosed as gallstones. Jean [10] cited six cases from the literature and reported one of his own, in which chronic jaundice was due to calcified nodes in the lesser omentum. Wakely [11] published the case of a man who complained of a lump in the stomach and dysphagia. Palpation of the abdomen revealed a hard, solid tumor about the size of an orange to the left of the epigastrium, easily movable as if in the mesentery. Operation revealed a large calcified lymph node. Still [1] described the case of a child, aged 5 years, who was operated on for the relief of abdominal pain and vomiting. At operation, a narrow fibrous adhesion was found, passing from a caseous mesenteric node to the ascending colon; under this adhesion a loop of ileum had slipped and had become strangulated. He cited a similar case in which the strangulating band passed from the node to the wall of the abdomen. One of the authors of this report recalls a case of intestinal obstruction in a child, aged 6 years. A mass was felt in the left upper quadrant. The diagnosis of the surgeon was intussusception. At operation, the intestine was

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4. Clute, H. M.: Enlarged Mesenteric Lymph Nodes, Boston M. & S. J. **183**:409-412 (Sept. 30) 1920.

5. Clute, H. M.: Difficulty in Distinguishing Between Urinary Stones and Calcified Abdominal Glands, Boston M. & S. J. **192**:151-162 (Jan. 22) 1925.

6. Valentin, E.: Der Ureterverschluss durch Mesenterialdrüsen Tuberkulose, Arch. f. klin. Chir. **118**:189-193, 1921.

7. Fowler, R. S.: Calcified Glands Proximal to the Common Bile Duct; Cysticoduodenal Ligament, Surg., Gynec. & Obst. **23**:718-719 (Dec.) 1916.

8. Mayo, W. J.: "Innocent" Gallstones a Myth, J. A. M. A. **56**:1021-1024 (April 8) 1911.

9. Ciaprini, G.: Tuberculous Glands Mistaken for Gallstones, Policlinico (sez. chir.) **31**:565-572 (Nov.) 1924.

10. Jean, G.: Chronic Jaundice from Tuberculous Glands in Lesser Omentum, Presse méd. **33**:38-39 (Jan. 10) 1925.

11. Wakely, C. P. G.: Calcified Glands of Unusual Size Giving Rise to Dysphagia, Brit. J. Surg. **10**:295-296 (Oct.) 1922.

found caught in adhesions passing from a mass of calcified tuberculous nodes. Jones [12] reported five cases in which intestinal obstruction made operation imperative. The condition found was tuberculosis of the mesenteric nodes. Blatt [13] states that tuberculosis of the mesenteric nodes can be diagnosed during life only when extensive.

The roentgen ray seems to have been used for diagnosis only by Clute,[4] Gehrels,[2] Lotsch,[14] and Carson.[15] Clute pointed out that the shadows of tuberculous nodes appear mottled, that motility can be demonstrated and that the passage of a catheter shows the nodes to be outside the urinary tract. Gehrels [2] advised that for the diagnosis of tuberculosis of the abdominal nodes, two roentgenograms be taken at intervals of several days. Lotsch [14] emphasized the importance of the use of the roentgenogram as an aid to diagnosis, but discussed neither the method used nor the characteristic findings. Carson [15] has written "In a few cases I have been able to obtain x-ray confirmation of the diagnosis, as a calcareous gland will throw a shadow—indeed in two cases it led to a diagnosis of a ureteric stone—but I think I have only once seen a vague shadow of a caseating mass."

SELECTION OF CASES FOR STUDY

In this study, a group of children was selected who were known to have been in contact with tuberculous persons or to be themselves subjects of tuberculosis. In order to eliminate those of the group not infected, an intradermal test with 0.02 mg. of tuberculin was performed in the case of each child. If the test proved negative, it was repeated with a dose of 0.1 mg., and, if necessary, with a final dose of 1.0 mg. If the tuberculin test proved positive, roentgenograms of the neck, chest and abdomen were taken as a routine procedure.

PREPARATION FOR ROENTGEN-RAY EXAMINATION

The technic used in examining the abdomen with the roentgen ray was a simple one. A flat plate (anteroposterior view) was first taken without previous preparation of the patient. If the roentgenogram showed the presence of deposits of lime salts, the patient was specially prepared and both a flat plate (anteroposterior view) of the abdomen and a lateral plate were taken. The preparation referred to consisted in

12. Jones, A. T.: Tuberculous Glands of the Mesentery, Am. J. Obst. **75**:417-426 (March) 1917.

13. Blatt, M. L.: Childhood Tuberculosis Lymphadenitis, Internat. clin. **1**:115, 1921.

14. Lotsch, F.: Die Tuberkulose der Mesenterialdrüsen, Klin. Wchnschr. **2**: 1892-1896 (Oct. 8) 1923.

15. Carson, H. W.: On the Clinical Aspects of Tuberculous Mesenteric Glands, Lancet **1**:869-872 (June 22) 1918.

doses of mineral oil (from 1 to 2 tablespoons) on five successive nights; on the fifth night, 1 grain of phenophthalein was given in addition. On the morning of the sixth day food was withheld and a soap suds enema was administered, four hours after which the roentgenograms were taken.[16]

Both flat and lateral roentgenograms of the abdomen were repeated at intervals of two to four weeks, in order to make sure that the shadows remained essentially the same and to note changes in the size or number of nodes.

DIAGNOSTIC CRITERIA

In order to make a diagnosis of calcification of the mesenteric lymph nodes by means of the roentgenogram, certain conditions must be fulfilled. The shadow cast by the nodes must have a characteristic appearance; the laterally taken plate must show that the shadows lie anterior to the bodies of the vertebrae; the shadows must persist in repeated plates in approximately the same positions and retain the same character.

The shadows of calcified lymph nodes, as usually seen, are oval, rounded or crescentic. They appear white[17] as contrasted with the shadows of the vertebral column, and are much more intense than the shadows cast by bone. It is a remarkable fact that the shadows of calcified nodes may stand out in detail when superimposed on the shadow of the much thicker vertebral column (figs. 1 and 2). The shadow of the calcified tuberculous node is not homogeneous, but exhibits variations in density, giving it an appearance which might be variously described as "mulberry-like," "honeycombed," "moth eaten," "mottled," "spotted" or "coarsely stippled." The periphery usually casts a shell-like shadow which is more dense than the shadow of the part within, but it is not itself homogeneous, being more intense (more heavily spotted) in some parts than in others. In some cases, the central portions of calcified nodes cast scarcely any shadows at all. Under these circumstances, the peripheries appear as circles or crescents with perhaps but one or two pinpoint spots representing the interior. The shadow of a tuberculous node forms a crescent when a part only of the outer portion is calcified.

16. After comparing a large series of plates taken with and without preparation, differences noted are so slight as to make us feel that preparation is unnecessary in the majority of cases. Preparation of the patient would be indicated if the shadows in the roentgenogram were not characteristic or if there were reasons to suspect that the mass might be fecal. If a mass can be palpated which cannot be seen in the roentgenogram, a second plate should be taken after preparation of the patient, in the hope that removal of air or material from the intestines might reveal the calcified nodes.

17. Shadows described as white refer to the appearance in roentgenograms. In photographs these shadows appear black.

In the majority of our cases, one could count one to five more or less sharply defined nodes in the roentgenograms of the abdomen. Shadows, however, were present in some plates in which a definite node outline was not discernible. These shadows must have been cast by nodes which were partially calcified and which, in consequence, gave very small, irreg-

Fig. 1.—Anteroposterior view of the abdomen, showing a group of calcified nodes overlying the vertebral column.

ularly shaped shadows (fig. 3). In some cases, small irregular shadows were jumbled together around a cluster or mass of well defined shadows of calcified nodes. Such shadows must represent lime salt deposits scattered about either in lymphoid tissue adjacent to the well defined calcified nodes or possibly in tuberculous exudate. This débris of lime salt

deposit, as it might be termed, has not been found in the absence of sharply defined nodes. The discrete nodes vary in size, as seen in the roentgenograms, from 2 to 3 mm. to 2 to 3 cm. in diameter. In the anteroposterior views, they are seen to lie to the right or left of the spine or to overlie the spine, most frequently at the levels of the fourth or fifth lumbar vertebrae. They are apt to be fairly close to the lateral processes. Some nodes, however, lay so far out from the spinal column that from the anteroposterior view of the abdomen alone, it was impossible to be certain that the calcified masses were not in the kidneys. The lateral view, however, shows that the shadows of the nodes must lie outside the kidneys, as they are situated anterior to the vertebral column. The lateral plate is, thus, of great importance in locating the position of

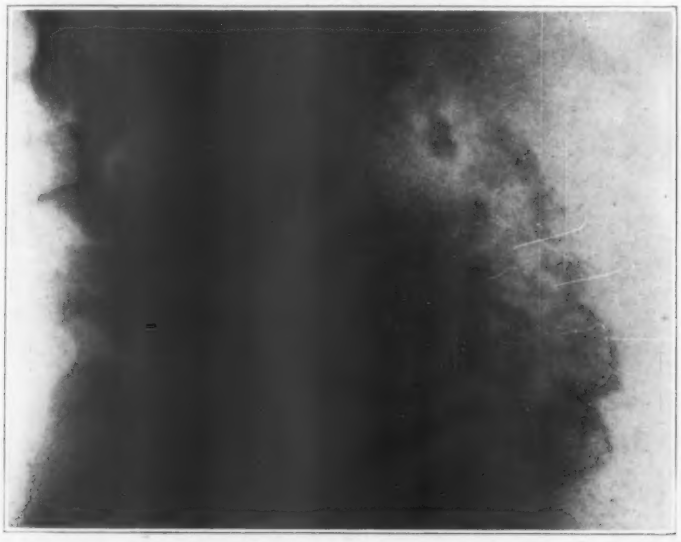

Fig. 2.—A lateral view of the abdomen. The nodes which overlie the vertebral column in figure 1 appear in figure 2 lying anterior to the vertebral column.

the nodes. Indeed, the calcified node or nodes may escape detection in the flat plate because they either overlie the vertebrae or lie so close to the lateral processes that their shadows are confused with the shadows of the latter (fig. 4). However, they show clearly in the lateral plate, in which there is no bony substance to obstruct the view or to detract from the contrast (fig. 5). The abdominal walls, the omentum, the mesentery and intestinal walls, being soft tissues, offer little resistance to the penetration of the rays. The gray shadow cast by these soft tissues is in sharp contrast to the snowy white of the calcified nodes.

There is no reason why shadows cast by fecal matter should ever be confounded with the shadows of calcified nodes, because fecal matter changes in position and can be removed. Moreover, the shadows cast by

masses of feces are not so white and lack the characteristic appearance of calcified nodes already described. In plates repeated at intervals of a week or two, fecal masses would have disappeared and new accumulations would not have the same appearance or occupy the same situations.

Contrary to the common belief, the abdomen seems to be a favorable part of the body for the roentgenographic demonstration of calcified lymph nodes as compared with the chest, in which the shadows cast by

Fig. 3.—Anteroposterior view of abdomen, showing a group of calcified lymph nodes with small irregularly shaped deposits of lime salts in the neighborhood.

sternum, ribs, heart, bronchi and great vessels may obscure the shadows of calcified nodes, lying as they do in the vicinity of the hilum of the lungs. The liver may hide from view nodes lying high up in the abdomen, and the true pelvis may conceal those low down, or the spine may conceal those in the median line. But the lateral plate will show nodes

lying in front of the spine, and, as already pointed out, the shadows of dense deposits of lime salts in nodes show clearly in roentgenograms against the shadows cast by bone. Moreover, tuberculous nodes are most commonly situated in the middle levels of the abdomen and are,

Fig. 4.—Anteroposterior view of the abdomen, showing two calcified nodes; the larger overlies the body of the third lumbar vertebra on the right side and the smaller overlies the tip of the lateral process of the same vertebra. These nodes might easily escape notice in the flat plate.

thus, usually not so high as to be lost in the shadow of the liver or so low as to be hidden by the shadow of the true pelvis.

In spite of the simplicity of the method for the diagnosis of tuberculosis of the abdominal lymph nodes, the roentgenogram does not seem to have been used systematically by any one as a regular diagnostic procedure.

SYMPTOMS

Tuberculosis of the mesenteric lymph nodes may cause symptoms, or may be an incidental finding in the course of a routine examination of a child seeming healthy or suffering from some unrelated condition. The finding of calcified lymph nodes in the abdomen, by means of the roentgenogram, does not mean active tuberculosis, nor does their absence in the roentgenogram mean that the lymph nodes of the abdomen are free from this disease. Symptoms may be caused by inflammation of lymph nodes not yet calcified; by tuberculous ulcers of the intestines, with associated localized involvements of the peritoneum, which drain into the infected nodes; by pressure of tuberculous nodes on adjacent structures, or by adhesions between nodes and intestine. Calcified lymph nodes may or may not be the seat of active tuberculosis.

Fig. 5.—A lateral view of the nodes shown in figure 4. The two nodes show clearly lying well in front of the vertebral body.

Their presence gives evidence merely of the existence of tuberculous infection, which may have become completely cut off from the rest of the body or which may be actively going on in the nodes themselves or in adjacent nodes or structures not revealed in the roentgenogram. Calcification in tuberculosis is commonly looked on as a conservative or protective process on the part of the body. When present in an abdominal node it probably means that the node has been the seat of tuberculosis for a considerable period of time, and, also, that probably there is, or has been, a tuberculous lesion in the intestine in the drainage area of the node. Symptoms of an inflammatory nature are presumably much more often referable to tuberculous ulcers or localized areas of peritonitis in the vicinity of the nodes than to tuberculous inflammations of the nodes themselves.

TABLE 1.—(Group 1).—*Children Brought to the Clinic Because They Were Ill*

Case	Name	Age in Years	Sex*	Exposure to Tuberculosis	Past History	Complaint and Present Illness	Physical Examination	Tuberculin Test	Roentgenogram of Abdomen: Antero-posterior	Roentgenogram of Abdomen: Lateral	Roentgenogram of Abdomen: Repeat	Other Evidence of Tuberculosis	Final Diagnosis
1	E. W.	8	♂	None known	Attack of abdominal pain 2 years previously	Attacks of abdominal pain accompanied by fever	Tender mass palpable left lower quadrant	+ 0.1 mg.	+	+	+	None	Tuberculosis of abdominal lymph nodes
2	A. R.	5	♂	Exposed several weeks to individual with active tuberculosis	Cervical lymphadenitis during previous winter	Sent to hospital with diagnosis of tumor of kidney	Large mass filling right side of abdomen	+ 0.1 mg.	+	+	Not taken	Tuberculous peritonitis found at operation	Tuberculosis of peritoneum and abdominal lymph nodes
3	E. C.	12½	♂	None known	Negative	Enuresis; difficulty in breathing	Tonsillitis; urine showed white blood cells, red blood cells, albumin and casts	+ 0.05 mg.	+	+	+	None	Acute nephritis; tuberculosis of abdominal lymph nodes
4	H. W.	7	♂	None known	Abdominal pain and diarrhea in 1924	Cramps, chills, vomiting, pallor	Spleen enlarged; mass palpable left lower quadrant	+ 0.1 mg.	+	Not taken	Not taken	None	Acute nephritis; tuberculosis of abdominal lymph nodes
5	A. W.	7	♀	Exposed to aunt with pulmonary tuberculosis	Had whooping cough three months before admission	Dry cough and run down condition following whooping cough	Pallor; underweight	+ 0.1 mg.	+	+	+	Tuberculosis of tracheobronchial lymph nodes by roentgenogram	Tuberculosis of abdominal and tracheobronchial lymph nodes
6	L. S.	6	♂	None known	Phlyctenule ? two years previously	Eye trouble	Negative except for eye condition	+ 0.1 mg.	+	+	+	Phlyctenular keratitis	Phlyctenular keratitis; tuberculosis of abdominal lymph nodes
7	S. P.	12	♀	Father died two years previously of tuberculosis	In hospital with attack of abdominal pain in June, 1924	Abdominal pain, vomiting, belching of gas; constipation	Palpable mass right lower quadrant; palpable thickened intestine	+ 0.02 mg.	+	Not taken	+	Probably intestinal tuberculosis	Tuberculosis of abdominal lymph nodes
8	E. N.	7	♂	None known	Negative	Nervousness and poor appetite	Negative	+ 0.1 mg.	+	+	+	Pulmonary tuberculosis by roentgenogram	Tuberculosis, pulmonary, and of abdominal lymph nodes
9	V. B.	10	♂	None known	Negative	Headache; pain in neck; vomiting	Signs of meningitis	+ 0.1 mg.	+	+	Not taken	Meningitis, tubercle bacilli in spinal fluid	Tuberculous meningitis; tuberculosis of abdominal lymph nodes
10	R. H.	5	♂	Father has pulmonary tuberculosis	Negative	Enuresis	Negative	+ 0.1 mg.	+	+	+	Pulmonary tuberculosis by roentgenogram	Tuberculosis, pulmonary, and of abdominal lymph nodes
11	L. S.	5	♂	Father has tuberculosis	Pneumonia	Attacks of coughing	Negative	+ 0.02 mg.	+	+	+	Roentgen-ray diagnosis of pulmonary tuberculosis	Tuberculosis of abdominal lymph nodes

* In this column, ♀ indicates female; ♂, male.

TABLE 2.—(Group 2.)—*Children Brought to the Clinic for Reexamination Because of Known Tuberculous Infection*

Case	Name	Age in Years	Sex*	Exposure to Tuberculosis	Past History	Complaint and Present Illness	Physical Examination	Tuberculin Test	Roentgenogram of Abdomen: Antero-posterior	Roentgenogram of Abdomen: Lateral	Roentgenogram of Abdomen: Repeat	Other Evidences of Tuberculosis
1	V. G.	9	♂	None known	Tuberculous peritonitis 1921	Came for examination on discharge from sanatorium	Palpable masses both sides of abdomen	+ 0.02 mg.	+	+	+	None
2	M. C.	8	♀	None known	Pulmonary tuberculosis 1921	Came for examination; had been in tuberculosis sanatorium	Negative	+	+	Not taken	Not taken	None
3	F. P.	6	♂	None known	Tuberculin positive 1922; tuberculous peritonitis	Came for examination; in tuberculosis sanatorium for one year	Negative	+ 0.02 mg.	+	+	+	Roentgen-ray diagnosis of tuberculosis of tracheobronchial nodes
4	S. T.	5	♂	None known	Cervical lymphadenitis; phlyctenular keratitis; pneumonia	Came for examination; no complaint	Negative	+ 0.02 mg.	+	+	+	Roentgen-ray diagnosis of pulmonary tuberculosis

* In this column, ♀ indicates female; ♂, male.

TABLE 3.—(Group 3.)—*Children with no Complaints Brought to the Clinic Because They Had Been in Close Contact with Individuals with Active Tuberculosis*

Case	Name	Age in Years	Sex*	Exposure to Tuberculosis	Past History	Complaint and Present Illness	Physical Examination	Tuberculin Test	Roentgenogram of Abdomen: Antero-posterior	Roentgenogram of Abdomen: Lateral	Roentgenogram of Abdomen: Repeat	Other Evidences of Tuberculosis
1	S. S	8	♂	None known	Negative	None	Negative	+ 0.1 mg.	+	+	+	None
2	M. S.	5	♀	Mother has tuberculosis	Negative	None	Negative	+ 0.1 mg.	+	Not taken	Not taken	None
3	J. F.	3½	♀	Father has tuberculosis	Negative	None	Negative	+ 0.1 mg.	+	+	+	None
4	B. H.	6	♂	None known	Phlyctenular keratitis November, 1922	None	Negative	+ 0.1 mg.	+	Not taken	Not taken	None
5	P. A	5	♂	None known	Occasional pain in abdomen	None	Negative	+ 0.02 mg.	+	Not taken	Not taken	None
6	J. N.	4	♀	None known	Negative	None	Negative	+ 0.02 mg.	+	Not taken	Not taken	Roentgen-ray diagnosis of pulmonary tuberculosis

* In this column, ♀ indicates female; ♂, male.

GROUPING OF CASES

In the course of this investigation 120 children were examined, of whom twenty-one, or 17 per cent, had tuberculosis of the abdominal lymph nodes. These twenty-one children may be divided into three groups: Group 1 consists of eleven children who came to the clinic because they were ill. The demonstration of calcified tuberculous lymph nodes in the abdomen was of value in making the diagnosis (table 1). Group 2 consists of four children who were known to have tuberculosis.

Fig. 6.—Anteroposterior view of the abdomen, showing a large calcified node on the left side at the level of the fourth and fifth lumbar vertebrae.

They had no complaints, but came for examination at the request of the physician (table 2). Group 3 consists of six children who were brought to the clinic because they had been in contact with persons with active tuberculosis. They had no complaints or symptoms. The demonstration of calcified abdominal nodes served to localize the site of a tuberculous infection (table 3).

REPORT OF CASES

GROUP 1.—*Case 1.*—E. W., a boy, aged 8 years, was admitted to the hospital on account of abdominal pain which had been present intermittently for five months, with occasional slight rises in temperature. Two years previously,

he had been admitted with a similar complaint, at which time a definite diagnosis was not made. At the present admission a mass could be felt in the left lower quadrant which was tender; this region was pointed to by the boy and described as "the place where I have my pain." The tuberculin test was positive. A flat plate of the abdomen (fig. 6) showed a calcified mass to the left of the spine at the level of the third and fourth lumbar vertebrae. A second plate taken six months later showed the mass in the same position and a lateral view showed it to be anterior to the spine (fig. 7).

GROUP 2.—*Case 1.*—V. G., a boy, aged 9 years, who had tuberculous peritonitis four years previously, on return from a sanatorium came to the New Haven Dispensary to be examined before going to school; he had no complaints. On examination of the abdomen several masses could be felt, and a roentgenogram showed numerous shadows of large calcified nodes having the characteristic honeycombed appearance (fig. 8). A lateral view showed these calcified masses to be situated in the anterior part of the abdomen.

Fig. 7.—A lateral view of the nodes shown in figure 6.

In the absence of symptoms, with gain in weight and no fever, the findings were interpreted as giving evidence of a healed tuberculous process.

GROUP 3.—*Case 1.*—S. S., a boy, aged 8 years, came to the clinic because his brother was known to have a positive tuberculin reaction. The child was well and had no complaints. The physical examination showed him to be slightly undernourished, but no evidences of tuberculosis were found. The tuberculin test was positive with 0.1 mg. A flat plate of the abdomen showed the presence of calcified lymph nodes on the right side at the level of the fourth and fifth lumbar vertebrae (fig. 9). A roentgenogram of the lungs was negative. In this case, the finding of calcified nodes in the abdomen localized at least one site of a tuberculous infection.

Tuberculosis of the mesenteric lymph nodes was demonstrated by roentgenogram in twenty-one of 120 children with positive tuberculin tests. Of these, six were girls and fifteen were boys. The youngest child was 3½, the oldest, 12½ years of age.

COMMENT

Although abdominal tuberculosis is considered by some to be usually of bovine origin, in nine cases there was a known human source of infection; in five cases the father was known to have tuberculosis and the child had been exposed in this way; in two cases the mother was suspected as the source of infection, but the diagnosis was not definitely established; one child was exposed through association with an aunt

Fig. 8.—Anteroposterior view of abdomen, showing large calcified nodes having the characteristic "honeycombed" appearance and present on both sides of the abdomen.

who had been in a sanatorium undergoing treatment for tuberculosis, and another through a sister. In the remaining twelve cases, the source of infection was unknown.

Only three children had symptoms referable to the abdomen, namely, pain and vomiting. The pain was described as intermittent and of a cramp-like, or colicky character. Other symptoms were belching of gas, fever, loss of weight, "tired feeling" and enlargement of the abdomen.

On physical examination a mass could be palpated in the abdomen in five, or 26.3 per cent, of the cases. The tuberculin test was positive in all cases.

Other evidences of tuberculosis besides the calcified abdominal nodes were present in thirteen cases. Pulmonary tuberculosis was diagnosed

Fig. 9.—Anteroposterior view of abdomen, showing a large mass of calcified nodes on the right side at the level of the transverse processes of the fourth and fifth lumbar vertebrae.

by roentgen ray in three cases and was suspected in two cases by the same means; the diagnosis of tuberculosis of the cervical nodes was made in two cases, and of the tracheobronchial nodes in two cases; of tuberculous peritonitis in one case, and of tuberculous meningitis in one case. In ten cases, there was a history of tuberculous peritonitis. Two

children had intestinal tuberculosis; in one the condition was diagnosed clinically, and in the other, at operation. One child had phlyctenular disease at the time of examination, and three children gave a history of having had it previously.

The child who had tuberculous meningitis died. One child is in a sanatorium and was doing well at last report. All the other children are living. Two underwent cystoscopic examination, and one child was submitted to an exploratory operation. In all the cases, the diagnosis was established or corroborated by roentgenograms of the abdomen.

Tuberculosis of the abdominal lymph nodes must be differentiated from a number of conditions, among which may be mentioned acute appendicitis, stone in the kidney or ureter, cholecystitis, tumors of the abdominal organs and lead poisoning (mentioned by Carson).

From the case reports, it is clear that tuberculous processes in the abdomen which affect the lymph nodes may simulate appendicitis. In these cases the pain appears to be less intense and of a colicky character. On palpation there may be tenderness, but muscle spasm seems to be less intense than in appendicitis. It is important to emphasize the fact that the finding of calcified abdominal lymph nodes in a patient with abdominal pain and vomiting does not rule out acute appendicitis, or mean, on the other hand, that the symptoms are caused by the tuberculous condition.

Also, patients with symptoms pointing to abnormal conditions in the urinary tract may show calcified masses in the abdomen which are not in the urinary tract and which are not the cause of the symptoms.

Tuberculous nodes may be so aggregated or joined together that they simulate tumors. The symptoms to which they give rise may serve merely to direct attention to the abdomen, and the discovery of tuberculosis of the abdominal lymph nodes may be the accidental result of the examination of the abdomen by means of the roentgen ray. Conversely, the tuberculous process in the abdomen may be the cause of symptoms and tuberculous nodes may be present, but may not be demonstrable by roentgenogram because not calcified.

SUMMARY

1. In a group of 120 children with positive tuberculin tests, twenty-one, or 17 per cent, had roentgenographic evidence of calcified tuberculous lymph nodes.

2. The shadows in the roentgenograms were of characteristic shape and appearance; in the lateral view they lay anterior to the vertebral column. They persisted in repeated plates and after evacuation of the intestinal contents.

3. The demonstration of calcified nodes in the abdomen is of value in establishing the locus of a tuberculous lesion; in helping to differentiate the condition from other acute abdominal conditions, such as appendicitis, sarcoma of the kidney, renal tuberculosis or stone in the kidney. By frequent repetition of abdominal plates, evidence should be obtained as to whether calcification is progressing or whether the calcified nodes are increasing or decreasing in size and number.

ARACHNODACTYLIA AND ITS ASSOCIATION WITH CONGENITAL HEART DISEASE

REPORT OF A CASE AND REVIEW OF THE LITERATURE*

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Arachnodactylia, or "spider digits," is a condition first described in 1896 by Marfan. It is characterized by the striking length and slenderness of the extremities, and differentiated from the gigantism of glandular dystrophy by the almost invariable accompaniment of congenital anomalies such as cardiac defects, webbing of the fingers, dislocation of the lenses, and many other conditions.

The condition was first brought to the attention of one of us by the late Dr. J. S. Fowler, who demonstrated the condition at the Royal Hospital for Sick Children, Edinburgh, in 1922. The case about to be reported is the second one seen by us and the eighteenth reported in literature. It has seemed worth while to publish an account of this condition as, so far as we know, there has been no previous mention of it in American medical literature.

CASE REPORT

B. S., a girl, aged 21 months, was admitted to the Children's Hospital on Sept. 20, 1925.

Family History.—The father was aged 22 and the mother aged 21 when the child was born. There were no other children in the family, and no other pregnancies had occurred. There was no history of tuberculosis, cardiac disease, syphilis, or of other congenital abnormalities.

Past History.—The patient was born on Jan. 1, 1924, at full term. Delivery was normal, but the child was blue at birth, and weighed 5 pounds (2.3 Kg.). For the first three months the baby was given Eagle Brand milk, then cow's milk, barley water and Karo. Later, Imperial Granum, malted milk, Eagle Brand milk, and Mellin's Food were used successively. At the age of 11 months, she was getting 24 ounces of milk, 8 ounces of water, and 7 tablespoons of Mellin's Food, 5 or 6 ounces every three hours. In addition, cod liver oil, cereal, egg and carrot were given. She did not finish her bottles. At 11 months, she could raise her head but could not sit up. Her first tooth came when she was 13 months old. Her weight at 14 months was 14½ pounds (6.4 Kg.). At 21 months, she could not lift her head or walk and said only one or two words.

Diseases.—The baby had bronchopneumonia at the age of 9½ months; tonsillitis, otitis media and pyelitis at 20 months. At the age of 11 months, she entered the University of California Hospital, when an operation was performed to repair a cleft palate; she did not have harelip. Two anesthetics of ether were given; during the first anesthetic, the patient became very cyanotic

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and artificial respiration had to be used. As a result of the operation, the soft palate was completely united, but the defect in the hard palate persisted. There was some fever for two days following the operation; otherwise the recovery was uneventful.

Present Illness.—The patient was brought into the outpatient department of the Children's Hospital because she was not gaining in weight as her mother thought she should. At that time, her weight was 14 pounds, 4 ounces, a gain of 5 pounds in sixteen months. The child could not sit up unsupported, and made no effort to pull herself into a sitting position. She could say a few words, according to the mother's report, but made no effort to talk while under observation. She was still entirely bottle fed, and was admitted to the hospital at this time for observation.

Physical Examination.—A rather emaciated, slightly cyanosed female baby, aged 21 months, weighing 15 pounds (average weight for age: 25 pounds) was observed. She did not appear ill, but displayed little interest in her surroundings, and made no attempt to sit up or to stand.

The hair was coarse, straight and abundant. The head was brachycephalic, with prominent frontal bosses and a rather flat occipital region; the anterior fontanel was depressed and admitted the tip of one finger. The greatest circumference was 43 cm., the normal for a child of that age being 46 cm. There was no evidence of deafness. The ears were round and simply convoluted, the lobule very deficient, and the eardrums on admission were normal. The expression was staring and unintelligent, the staring expression being due to deficiency of the lower eyelid. The eyes were rather deep-set and the epicanthic folds slightly exaggerated, while the lower eyelashes were extremely scanty. The external ocular muscles showed nothing abnormal; the pupils were very small and round and reacted slowly but equally to light. No eyeground examination was made. The eyes followed a light and evidently could see. Apart from the very flattened bridge and the small size, the nose appeared normal. In the mouth, six upper and four lower teeth were present, but irregular. The palate was highly arched and showed a central opening, confined to the hard palate and associated with some deviation of the uvula. (The child had had one Brophy operation.) The tonsils were moderately enlarged. The neck was normal except for thinness, moderate venous pulsation, and slight adenopathy.

The chest appeared very narrow, and the circumference measured 7 cm. less than that of the normal child of the same age. Respirations were abdominal in type. Sternum, clavicles and scapulae were not extraordinary, but a slight precordial bulging was noticeable. The heart had visible pulsations to the left of the sternum in the third and fourth left spaces; the apex beat was both visible and palpable in the fifth left intercostal space, 7.5 cm. from the median plane. A systolic thrill was present, and was felt in the second and third left interspaces close to the sternum. A loud, basal murmur was audible on both sides of the sternum, quite distinct in both supraclavicular fossae, almost inaudible over the apex, but extremely distinct over the chest posteriorly. The murmur began in late diastole, just before the first sound, and continued throughout almost the entire systole, but did not replace the first sound. The pulmonic second sound was accentuated.

Peripheral Circulation.—Very slight cyanosis was definitely present. The extremities showed no true clubbing. The pulse varied between 120 and 130, with marked sinus arrhythmia.

Lungs.—On admission, the lungs were considered normal.

Abdomen.—The spleen was felt 1 cm. below the costal margin. Subcutaneous fat was deficient. The genitalia were normal.

Back and Extremities.—No scoliosis was present, but a dorsal lumbar kyphosis was fairly marked. The arms and legs seemed extremely long, slender and awkward. The impression of length was partly spurious, however,

being due probably to the extreme slenderness, as actual measurements showed little difference from the normal. No paralysis was present, though the child was able to move the arms and legs only fairly well and could not grasp objects. The arms were freely movable at the shoulders, while at the elbows the forearms could not be completely extended. The hands were markedly deviated to the ulnar side, and the fingers, which were kept flexed, were long, bony and clawlike, with a slight degree of webbing. The middle digit measured 4.5 cm. in length, and the fifth digit showed a slight exaggerated curving, but without the shortness of a mongolian digit. The feet were long and the heel projected backward, thus accentuating the length. The toes were long, particularly at the first phalanx. Movement was fairly free in all directions, and the knee joints were somewhat hypotonic. Coordination was poor, and occasional tremors of the hands were noted.

Reflexes.—The patellar reflexes were sluggish. The abdominal and supinator reflexes were not obtained. No clonus was present, and Babinski's sign was negative.

Skin.—This was dry and fine, and subcutaneous fat everywhere was rather deficient.

Glands.—Apart from the slight cervical adenopathy, there was no glandular enlargement.

Measurements of the Child with Reference to Normal Measurements for the Same Age

	No. of Tarsal Bones	Leg: Ant. Sup. Spine to Med. Malleolus, Cm.	Arm: Acromion Process to Tip of Middle Digit, Cm.	Finger: Web to Tip, Cm.	Foot: Entire Length, Cm.	Head: Circumference Occipitofrontal, Cm.	Chest: Circumference at 4th Rib in Midax. Line, Cm.	Weight of Baby, Pounds	Total Length Baby, Cm.
Baby S.....	3	39.5	28.5	4.5	11.5	43	39	15	78
Normal child of same age.....	3	34	31	3.5	12	46	46	25	79
Normal child of same weight...	2	26	25	3.2	9.5	42.2	Holt 41	15.5	Holt 63.6

Laboratory Work.—The Wassermann reaction was negative for both the mother and the child. The blood count showed red blood cells, 6,530,000; hemoglobin (Sahli), 55 per cent; white blood cells, 16,700; polymorphonuclears, 36 per cent; lymphocytes, 64 per cent. Urinalysis on admission was negative.

Roentgen-Ray Report. (Dr. Cook).—"The heart is considerably enlarged to the left. There is no prominence in the pulmonic area, the enlargement being mainly in the left ventricle. There is extensive fibrous thickening in the central portion of the right lung field." The roentgen-ray diagnosis was that of a congenitally diseased heart and chronic pulmonary fibrosis. The plates of the extremities showed three bones in the tarsus (two or three are normal). Rarefaction of the bones was moderate, and involved especially the rib cage and scapulae.

The electrocardiogram showed a rate of 130, with sino-auricular tachycardia and a slight increase of the left axis deviation. Dr. Sampson considered that this was not definitely pathologic but that it was consistent with a congenitally diseased heart.

During the greater part of the infant's stay in the hospital, her temperature ranged between 99 and 100.5 F., the cause of which was not apparent. On October 12, left otitis media was diagnosed and paracentesis was performed. The temperature at the time of the operation had risen to 104.5 F., and remained elevated during the following four days. A moderate pyuria was present, and on October 17, high-pitched breath sounds with diminished resonance were found

in the right axilla. Cyanosis was at this time an intermittent symptom. On October 18 the temperature was 108.8 F., and the child became rapidly worse and died.

The clinical diagnoses were: (1) arachnodactylia; (2) a congenitally diseased heart, questioned patent interventricular septum; (3) cleft palate; (4) multiple congenital stigmas; (5) mental retardation; (6) otitis media; (7) pyelitis; (8) bronchopneumonia.

Necropsy Findings.—"The remains are those of a child, female, aged 2 years. The body is slender, undernourished and cold.

"Head: The hair is abundant and coarse. The anterior fontanel is almost closed and posterior fontanel is closed. The parietal and frontal bosses are prominent. The temporal regions are flattened. The eyes are slightly narrowed, pupils are small, and there are scarcely any lower lashes. The nose is flattened. The ears are rounded and the lobule is small. The mouth shows a slit 1.5 cm. long in the hard palate and an opening in the soft palate 1 by 1 cm. and slightly to the left of the middle line. The mucous membranes are pale. In the neck, small posterior glands are palpable.

"The chest is negative externally. The abdomen shows slight distention. The genitalia are negative. Cyanosis of the finger nails is present, and the little finger on both sides is bowed with the convexity toward the ring finger.

"Ventral incision shows little subcutaneous fat. In the abdomen, the round ligament and urachus are negative. The organs are in their normal position and the intestines are distended with gas.

"Chest: There is no fluid in the right pleural cavity, while in the left there is 10 cc. of blood tinged fluid. The left lung is collapsed, and appears as a single lobe with very slight indication of division. Patches of bronchopneumonia are present. The right lung feels firm, and there are no pleural adhesions. The upper lobe is emphysematous; the lower lobe is congested and a reddish purple in color. Section of the upper lobe shows a reddish, mottled appearance, while section of the lower lobe shows bronchopneumonia. The middle lobe is extremely small.

"Heart: The right auricle is dilated, the right ventricle is dilated, the left auricle and ventricle are negative. The valves appear negative. The mitral valve measures 4.4 cm.; the tricuspid valve measures 4.2 cm. There is a deficiency of the interauricular septum involving both septum primum and septum secundum, which measures about 1.5 cm. across. The aorta is negative.

"The genito-urinary and gastro-intestinal systems are negative.

"The brain shows slight internal and external hydrocephalus, involving especially the posterior horn of the lateral ventricle. The ependyma and choroid are negative. The hypophysis is normal. Microscopically, there is slight disarrangement of the cell layers, especially in the frontal lobes.

"Microscopically, the kidney shows cloudy swelling of the tubules. The spleen is markedly congested with red blood cells. The liver shows a moderate increase in fat content and some passive congestion. Congestion of the capillaries of the lungs is extreme. There are a few areas of inflammatory exudate into the alveoli, and some areas of peribronchiolar inflammation.

"Pathologist's Diagnosis: (1) Bronchopneumonia and left hydrothorax; (2) dilatation of the right side of the heart, and deficiency of the interauricular septum; (3) anomalies of division of both lungs, of the ears, eyes, palate and extremities; (4) emaciation."

COMMENT

Chief Features of the Condition.—It will be seen on reviewing the other cases in the literature that the one just described shows many of the salient characteristics. The family history was negative in all but one case, that of Achard,[1] in which

1. Achard, M. C.: Bull. et mém. Soc. méd. d. hôp. de Paris **19**:834-840, 1902.

abnormally large extremities were present in the parents and in which the diagnosis was open to question. In two instances, however, other members of the family were the subjects of unrelated congenital deformities. Whether any sex influence is present is doubtful. Eleven of the subjects were female, and six were male. In ten cases, the baby was noted to be abnormal at birth, and in seven of those cases the extremities showed extreme slenderness at birth. Development of these children seems to be approximately normal, though slow in some details. This retardation of development is largely due to physical disability and weakness. Only three children were noted to be backward mentally; of these, one subsequently became quite normal. Infections seem to be of about average incidence in those children, two other subjects showing, like our subject, a tendency to respiratory infection.

The weight and height of many of the patients are striking, seven of them being much above the average height, one being short, and the others being approximately normal. In all the cases in which the weight is mentioned, the subjects varied between 2 and 18 pounds underweight, the average being 10 pounds below normal.

In nine of the cases the musculature is described as being poor, atrophic or wasted. Electrical reactions were attempted in only two cases; one of these showed a perfectly normal response while the other showed a diminished reaction to faradism. Contractures of the flexures of elbows, knees, fingers, hips and spine constitute a prominent feature in eleven of the cases, while hyperextensibility, affecting chiefly ankles and wrists, is described in five cases.

No agreement is possible as to any characteristic shape of the head in this condition, though in nine cases it is noted as abnormal. Dolichocephaly and asymmetry are the most common findings; brachycephaly occurred only in our case. The hair is described as coarse in three cases, and in ten cases anomalies of the eyes are emphasized. In these cases, the eyes were deep-set and showed contracted pupils and trembling irises. Dislocation of the lens was noted in five cases; while occurring less frequently, we find lenticular opacity, nystagmus, and, in our case, a defect of the lower eyelids and eyelashes. In about half the cases, anomalies of the ears are present. Cleft palate was noted in only one case.

The chest showed varying deformities in eight cases, and was characterized chiefly by its narrowness and flatness. Clinically, the lungs were normal in most of the cases, but in the two cases in which necropsy notes are available, a striking similarity in the lung findings is obtained. Both patients died of pneumonia, and in both of them congenital defects of the lungs were found. In Börger's [2] case, the middle

2. Börger: Ztschr. f. Kinderh. **12**:161, 1914.

lobe of the right lung was represented by a small tongue-like process on the lower aspect of the upper lobe. The left lung showed a very large lingula. In our case, the middle lobe was extremely small, and there was little evidence of division of the left lung into its two lobes.

With fair constancy, the spine showed either kyphosis (as in the case described by Rocher [3]) or scoliosis, or both. The condition does not seem to be merely dependent on the poor musculature and, consequently, postural defects, as three of the babies in which it was pronounced had made no attempt at sitting, standing, or holding up the head.

It is with the extremities particularly that we are concerned in the diagnosis of the condition, and certain characteristics are common to all cases described. In every instance, the length and slenderness of the extremities were noteworthy. This lengthening was emphasized by Dubois,[4] by Achard,[1] and by Dupérié,[5] in whose cases the length and slenderness became more striking the more distal was the part examined. It is to this feature that the condition owes its name of "spider digits," because, though trunk and long bones are distinctly abnormal, the striking features are the long narrow hands and feet and the slim, spidery, contracted phalanges. In six of the cases, the heel was noted as projecting backward, three cases showed webbing of the fingers, while hammer-toe, presumably a form of contracture, was present in two of the series.

The roentgenograms showed three characteristics of the condition, namely, rarefaction of the bones, spurring of the os calcis, and advancement of the ossification. In all cases in which the sella turcica is mentioned, it is normal. This last observation is of importance when one comes to consider the etiology of arachnodactylia.

The Heart.—Along with the characteristic form of the extremities, the contractures, and the anomalies of the eyes, one must consider congenital heart disease as one of the classical accompaniments of the condition. In ten of the cases, the heart was either left undescribed or considered normal. In the remaining eight cases, murmurs and cardiac enlargement were described. The notes on many of the cases are scanty, so that a definite conclusion cannot be reached with any readiness in determining whether the lesions were congenital, acquired, or merely of functional origin. In five of the cases, a definite diagnosis of congenital cardiac defect was made; in one case it was presumptive, while the remaining two cases were considered noncongenital. Poynton and Maurice [6] ascribed a loud systolic murmur to an attack of tonsillitis;

3. Rocher: J. de méd. de Bordeaux **29**:52, 1920.
4. Dubois: Ztschr. f. Kinderh. **5**:401 (Aug. 5) 1912.
5. Dupérié, R.; Dubourg, E., and Guénord, F.: J. de méd. de Bordeaux **92**:43, 1921.
6. Poynton and Maurice: Tr. M. Soc. **45**:21, 1923.

and Ormond considered the pulmonic bruit of his patient to be of functional origin.

In three of the cases recorded, permission for necropsy was obtained. Unfortunately, Pfaundler [7] does not mention the cardiac findings, and merely states that no demonstrable lesion of the endocrine glands was discovered. Börger, however, goes into more detail and describes the cardiac defect to be due, in his case, to patency of the foramen ovale. In our case, although a diagnosis of the lesion was not made before death, the clinical findings tally with those given by Maude Abbott as characteristic of a defect in the interauricular septum. The murmur was presystolic and systolic, and varied in intensity and location. The thrill was not localized but was felt over the upper precordium generally, and the cyanosis, which was slight throughout life, became suddenly aggravated just before death. Both electrocardiogram and 2 meter heart plate, though abnormal, were not pathognomonic. It is unfortunate that in the remaining cases so little attention was paid to the cardiac condition, for, on reviewing the literature, the frequency of congenital heart disease becomes one of the prominent features of arachnodactylia. It is interesting that in the only two cases examined at necropsy, a similar cardiac defect should be found.

THE ETIOLOGY AND PATHOLOGY OF THE CONDITION

Little that is convincing has been contributed to our knowledge of the etiology of this condition. There are no factors in race, in family history, in the health or age of the parents that are characteristic. The Wassermann and tuberculin reactions were negative in those patients on whom they were made.

Poynton [8] and Thursfield have considered the condition to be possibly a form of infantile muscular dystrophy. The latter admits that the undue length and slenderness of the extremities do not occur in the myotonias. The clinical picture is not merely that of a disease of the muscles with atrophy, hypotonia and contractures, but a disease affecting the most varied structures and not necessarily the muscles at all, as in the case reported by Thomas,[9] in which the muscles were normal. Electrical reactions were done in only two of the cases. One of these (Marfan's [10]) showed a normal electrical response, while Dubois' patient showed a slight diminution of reaction to the faradic current. The muscular findings, therefore, are not sufficiently constant or striking to hold them responsible for the condition.

That the condition is analogous to mongolism has also been suggested by Thomas [11] and Thursfield,[12] and, indeed, in a few respects the case

7. Pfaundler: Abstr. in München. med. Wchnschr. **56**:280, 1914.
8. Poynton, F. S.: Tr. M. Soc. **26**:338, 1903.
9. Thomas: Ztschr. f. Kinderh. **5**:401, 1912.
10. Marfan, B. J. A.: Bull. et mém. Soc. méd. d. hôp. de Paris **8**:220, 1896.
11. Thomas: Ztschr. f. Kinderh. **52**:109, 1914.
12. Thursfield: St. Bartholomew's Hosp. Rep. **53**:35, 1917.

which we are reporting resembles a mongol, the small brachycephalic head, the prominence of the epicanthic folds, and the curved fifth digit, which, however, lacks the shortness of the mongolian digit. The general appearance of the baby, the straight setting of its deep-set eyes, and the long, bony extremities do not suggest mongolism, and it will be remembered that dolichocephaly was the most common cranial shape found in the other subjects. The mentality ranged from slight backwardness to exceptional intelligence, most of the patients being mentally normal.

Several writers have brought forth arguments to classify the condition as a type of glandular dystrophy, and have suggested the pituitary as the gland probably affected. In support of this statement, one patient of the series, an indubitable case of arachnodactylia, is thought to have improved with polyglandular treatment. Roentgenograms of the sella have been negative in all eight cases of the series in which such plates were taken. The necropsy findings in our case were negative so far as the hypophysis was concerned, while Börger found multiple small cysts in the anterior lobe of the pituitary, the posterior lobe being normal. In another connection, Park and Powers [13] have maintained that the embryo is dependent for proper growth and development not on its own, but on the parental organs of internal secretion. True acromegaly in infancy has very definite characteristics, as in the case reported by Salle,[14] when, in addition to long extremities, the baby showed a prominent chin, long nose, macroglossia and edematous eyelids. The condition was not noted at birth, but was rapidly fatal, and at necropsy definite changes were found in the hypophysis.

Börger looks on the condition as a "partial gigantism caused by defective anlage of the entire organism and perhaps early intra-uterine exhaustion, especially of endocrine glands."

To us, the last seems perhaps the most convincing view as to the etiology, though we have no suggestive history to lend strength to such a theory. A disease entity with so many and such varied manifestations must necessarily be due to some pathology of the germ plasm occurring at the earliest stages of embryonic life, when dependence on the maternal organism is complete. The emaciation, the slenderness, the advanced ossification and old appearance of the subjects may possibly be due to the effect of an accompanying early nutritional defect in the embryo, bringing about a congenital variety of that occurring to a less marked extent in acquired malnutrition.

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13. Park, E. A., and Powers, G. F.: Acrocephaly and Scaphocephaly with Symmetrically Distributed Malformations of Extremities, Am. J. Dis. Child. **20**:269 (Oct.) 1920.

14. Salle: Jahrb. f. Kinderh. **75**:540, 1912.

MORBID ANATOMY IN A CASE OF DIABETES

WITH ONSET AT THE AGE OF EIGHT MONTHS*

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In this journal, in the September, 1925, issue, Dr. Schippers reported a case of "Diabetes Mellitus in an Infant Aged Eight Months Treated with Insulin." The child died at the age of 2 years and 2 months. She stayed at the hospital until her death and the diagnosis of diabetes mellitus, made after careful clinical observation, cannot be doubted. Coma set in after a pharyngeal infection. Three days before death, the body weight was 11.8 Kg.

Necropsy (performed by Dr. Schippers).—The body was that of a well nourished child. Rigor mortis and livores mortis were present. The subcutaneous fat layer of the abdominal wall measured 10 by 12 mm. The muscles were dark red. The abdominal cavity contained a small quantity of clear, dark yellow fluid. In the omentum, the mesentery and surrounding the kidneys, large masses of fat were seen. The weight of the thymus gland was 10 Gm., of the thyroid gland almost 2 Gm. The heart presented no anomalies except for a slight degeneration of the muscle. There was a small focus of pneumonia in the lower lobe of the left lung; there also was some hypostasis, edema and bronchitis. The right upper lobe showed numerous subpleural hemorrhages, some small spots of pneumonia and mucopurulent bronchitis; the middle and the upper lobe were only slightly affected. At the bifurcation of the trachea a caseous lymph node was found.

The mesocolon of the colon transversum was quite short. The lymph glands were not enlarged. The veins in the abdomen were engorged with blood, in particular those around the pancreas. The latter appeared normal macroscopically, and weighed 7.6 Gm.

The liver was hyperemic and had yellow brown spots, and fatty degeneration; its weight was 350 Gm. The spleen looked normal, its weight was 20 Gm. The suprarenals were yellow, the right weighed 4.5, the left 3.5 Gm. The cortex of the kidneys was swollen; they looked pale and their markings were no longer clearly visible. The weight of the right kidney was 46 Gm.; that of the left 40 Gm. The ovaries appeared like ivory balls; the right one measured 29 by 7 by 4 mm., the left measured 22 by 12 by 4 mm. Brain section was not permitted.

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* From the Emma Hospital for Sick Children.

Before giving the microscopic description of the organs, the foregoing findings will be discussed. The positive Pirquet test during life was accounted for by the caseous lymph gland, the only focus of tuberculosis which could be found. The weight of the pancreas was rather low, the average for this age being about 11 Gm. (Nakamura [1]). However, the weight of the spleen and the liver were also low for a well-nourished child. The kidneys were large and had increased in weight. The thymus gland was above the average and the thyroid gland was a little below the average for this age. The suprarenals might be called hypertrophic. This is interesting, since Kraus [2] found regularly atrophy of the suprarenals in young diabetic patients (the youngest being 14 years old). Large kidneys are a common finding in diabetes.

In a recent article, Kraus has drawn attention to the study of the other endocrine organs in diabetes. In young persons he could always find a decrease in weight of the hypophysis cerebri and a diminution of its oxyphil cells in number and in size; atrophy of the suprarenals with, in most cases, atrophic and degenerative processes in the cortex (the relation between cortex and medulla being generally not modified), atrophy of the parathyroid bodies, a struma colloides and more or less change in the genital organs. He emphatically states that he regards these findings as secondary to the pancreatic lesions, but, according to his point of view, pancreas, suprarenals, thyroid, hypophysis and parathyroid bodies are links in the sugar metabolism, which influence one another partly in a stimulating, partly in a depressing sense.

In our case, besides the pancreas, I have examined the thyroid and thymus glands, the suprarenals and the ovaries. The hypophysis cerebri was not available, and the parathyroid bodies were not looked for at the section. Preparations were also made of the liver, spleen and kidneys.

Microscopic Examination.—Thyroid Gland: The septal connective tissue had somewhat increased. The size of the vesicles varied greatly; [3] some were very large. In some spots little groups of lymphoid cells were seen. There was much colloid.

The thymus gland showed the usual findings.

Suprarenals: The cortex was well developed and showed neither fatty degeneration nor narrowing. The medulla, however, was only a thin layer with few chromaffin cells.

Ovaries: There were numerous primordial ovula and beginning follicles. The spleen was normal.

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1. Nakamura, Nobu: Virchows Arch. f. path. Anat. **253**:286, 1924.
2. Kraus, E. J.: Virchows Arch. f. path. Anat. **247**:1, 1923.
3. At the age of 2 years, there is still much difference in the size of the vesicles. Cooper, Eugenia R. A.: The Histology of the More Important Human Endocrine Organs at Various Ages, Oxford Medical Publications, 1925.

Liver: There was fatty degeneration of a great deal of parenchyma, but not of the cells of Kupfer. There were large quantities of glycogen in the liver cells and in the perivascular sheaths. There was also some nuclear glycogen. (In general, the liver of diabetic patients who die in coma is devoid or almost devoid of glycogen.)

Kidneys: Just beneath the capsule, some hyaline malpighian bodies were seen. The nuclei in the glomeruli had increased in number. Compared with preparations of kidneys from children of the same age, the malpighian tufts in diabetes did not seem enlarged. The first part of the tubuli contorti was somewhat swollen. The kidneys contained much less glycogen than was expected; however, it was present in several spots in the loops of Henle and in the connecting tubules. A remarkable fact was the presence of small droplets of glycogen lying free in the interior of the capsule of Bowman and in the lumen of the renal tubuli. According to some authors, this fact proves that the glycogen in loco is derived from the blood sugar. We must, however, be very cautious in our deductions, as it is well known that the histologic technic can remove the glycogen from its original place.

Pancreas: The microscopic investigation of the pancreas was of great interest in this case. To my knowledge, in the literature there are only two cases of diabetes in infants in whom a necropsy was made One of them was described by Cuno,[4] the other by Kochmann.[5] Another interesting point is that our patient was treated with insulin for a period of seventeen months. In practice, an increase of the sugar tolerance under the insulin treatment is sometimes noted. In these cases a regeneration of islets in the pancreas might be visible. Our patient showed slight sugar tolerance, though only for a brief space of time.

The discovery of insulin has placed the islets of Langerhans in the center of interest, and several authors are of the opinion, that no real diabetes is found with intact insulae. One cannot draw a sharp line of separation between the changes in the pancreas in older people and those in young ones, but in general it may be said that the latter often present elective insular lesions, whereas in older people there is often cirrhosis and lipomatosis of the pancreas with secondary lesions of the islets.

In order to gain an accurate picture of the structure of the pancreas in our case, three pieces of the caput, three of the corpus and three of the cauda were imbedded in paraffin and cut into 10 micron sections. Of these sections fifty were examined in such a way that between the sections that were kept and stained, several were discarded. The parenchyma was normal. The connective tissue between and in the lobules had not increased, neither had it undergone hyaline degeneration. No

4. Cuno, F.: Klin.-therap. Wchnschr. 1911.
5. Kochmann, R.: Jahrb. f. Kinderh. **99**:20, 1922.

traces of an inflammatory process could be detected in the gland. In the islets, there was neither hyaline nor hydropic degeneration, nor was there necrosis, sclerosis, calcification or lipomatosis (with one exception, as I saw fat in one islet). Some "free insulae" could be found, but according to Nakamura [1] they are present up to the fourth year and their number had certainly not increased. The same holds true for the very small islets composed of two kinds of cells and situated near small ducts; therefore, regeneration of islets could not be discovered. Some giant forms could be seen. The pancreas of young children contains many small islets, as Nakamura states, and as my own control preparations of the pancreas of a child of the same age and of three younger children proved.

NORMAL OR SUBNORMAL ISLETS

It is difficult to ascertain whether the size and the number of the islets is normal or subnormal, if the deficiency is not very marked, as there is a rather large physiologic variation. I tried in the following way to obtain an objective opinion. With the drawing apparatus of Zeiss, the circumference of 150 islets (50 caput, 50 corpus, 50 cauda) was taken, and small pieces of paper were cut out with a pair of fine pointed scissors and their weight taken. The same was done with 150 islets of control preparations of the pancreas of a child of the same age, who died of pneumonia. In the diabetic child the weight of the paper islets was 1.275 Gm.; in the control pancreas, 0.910 Gm. To obtain an idea of the number, I counted microscopically the islets in 60 fields (low power magnification), 20 fields for the caput, 20 for the corpus and 20 for the cauda and found them to be 835 in the diabetic and 946 in the child who died of pneumonia. In both cases there was a marked difference in size between the various islets; often one islet was 10 times the size of its neighbor. Again, the number of islets that are found in the following fields of the microscope differs greatly. As far as this investigation permits a conclusion, one may say that the anatomic structure of the pancreas in this diabetic child was normal. It is true that the weight of the whole gland was less than normal, but we all know from the experiments of von Mehring and Minkowsky in dogs, that if only one fiftieth of the pancreas was left in the body of the animal, diabetes did not occur. Kraus also reports a case of diabetes, in which the islets were practically normal.

QUANTITY OF THE ISLANDS OF LANGERHANS

Some skeptical authors state that every pathologic process found in the diabetic pancreas may also be seen now and then in the normal gland. It is also of great interest that Nakamura noted atrophy of the islets of Langerhans in infants suffering from gastro-intestinal dis-

turbances and other illnesses leading to marasmus, and from acute toxic infectious diseases. In rare cases he even saw the intrainsular connective tissue broader and more homogeneous than usual, and a hydropic degeneration of the islands, which is described as being pathognomonic for the diabetes of old people. Nakamura is of the opinion that the quantity and not the quality of the islets decides whether diabetes will occur, whereas de Josselin de Jong [6] in his recent publication says that the alterations found in the islets are primarily in quality and then in number.

That the islets of Langerhans play a part, all of us are willing to believe, and the benefits derived from the insulin treatment prove this fact, but in our case and in others mentioned in the literature, in which only slight pancreatic lesions were present, it is highly probable that the primary cause of the illness is not situated in the pancreas and that the secretion of the insular hormones is dependent on the function of certain as yet partly unknown cerebral centers.

BRAIN PATHOLOGY

Until lately, examination of the brain in diabetes has not increased our knowledge, but the investigations of Dresel and Lewy [7] and the experiments of Camus, Gournay and Le Grand [8] make it necessary in the future to examine the brain in serial sections.

In four cases of diabetes, the first cited authors found on both sides a circumscribed pathologic focus in the globus pallidus, the nuclei paraventriculares being intact. They presume that the paraventricular nuclei are subject to a regulating influence of the globus pallidus.

Contrary to Cushing's experiments, Camus, Gournay and Le Grand could not determine an influence of the hypophysis cerebri on the sugar metabolism, but lesions in the region of the tuber cinereum produced glycosuria of several weeks duration in rabbits and dogs. On examining the brain of the animals in serial sections, they always found the nuclei paraventriculares and the nuclei proprii of the tuber affected.

That our patient did not suffer from a cerebral tumor, hydrocephalus or meningitis may be taken for granted, but we must not forget that, on admission, the child showed some symptoms pointing to a cerebral condition (encephalitis?). It is regrettable that brain section was not possible. Our patient, with a practically normal pancreas, may be a stimulus for examination of the brain in diabetes.

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6. De Jong, de Josselin, quoted by van den Bergh, Hymans: Voordrachten over Suikerziekte, Oosthoek, Utrecht, 1925.

7. Dresel and Lewy: Thirty-third Kongress der deutschen Gesellschaft für innere Medizin, Wiesbaden, 1921.

8. Camus, J.; Gournay, J. J., and Le Grand, A.: Presse méd. **33**:249 (Feb. 25) 1925.

CONCLUSION

In conclusion, I will mention briefly the cases of Cuno and Kochmann.

Case of Cuno.—A child, admitted to the hospital at the age of 15 days, died of atrophy and bronchopneumonia after a week. Sugar was constantly found, but not more than 0.3 per cent. There were no other symptoms of diabetes, and no coma. The weight of the pancreas was 1.5 Gm. Microscopic findings showed cirrhosis; the islets seemed normal. The author regards the case as one of pancreatic diabetes, at least as one of pancreatic glycosuria.

Case of Kochmann.—A patient entered the hospital at the age of 4½ months, with a body weight of 3,475 Gm. He was under clinical observation until death, at the age of 8 months. The diagnosis of diabetes must be accepted. Necropsy was performed by Professor Ceelen. The weight of the pancreas was 2.6 Gm.; there was fatty degeneration of the parenchyma. The islets were few in number (no histologic details of the islets are given). There was proliferation of the connective tissue over the whole gland, partly with numerous groups of lymphoid cells and greatly increased number of spindle cells. In the cauda of the pancreas, lymphoid nodules were seen. In the middle lobe of the hypophysis cerebri was a rather large cyst. Edema of the pia and brain, and thrombosis of the right sinus transversus were present. Round cell infiltration of the pia was present. In the brain there was nothing abnormal ("Gehirn ohne Befund"), but I do not suppose it was examined in serial sections.

The case of Kochmann is interesting, and various questions present themselves which are not answered by the author. For instance, the description of the histologic findings in the pancreas points to an inflammatory process. One would like to know if the child suffered from an acute infectious disease. The lymphadenomatous tissue found in the gland may be explained by an exudative diathesis, as can the large follicles of the spleen. One would like to know whether there were alterations in the region of the tuber cinereum, which perhaps in this case might have been found.

FEVER IN THE NEW-BORN INFANT*

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MINNEAPOLIS

The production of body heat at a rate sufficient to offset its inevitable loss, and thus to maintain the body temperature at a constant level is necessary for every warm blooded animal. This function apparently is not fully developed until about the time of birth, for with infants born prematurely, external heat must be applied in order to sustain the body temperature at the normal level. After the ability to maintain a normal temperature has been acquired, minor fluctuations occur, which, according to Benedict and Talbot,[1] amount to about 0.33 C. during the first eight days of postnatal life.

VARIATIONS IN TEMPERATURE

Variations in normal temperature at different ages are very slight It is known, however, that the temperature of the fetus is slightly higher than the rectal temperature of the mother. This difference results from the fetus having a certain metabolism of its own, and its surrounding in the warmest organ of the mother's body. Immediately following birth, the rectal temperature of the infant falls from 1 to 3 degrees, the extent of the decline depending on the length of time elapsing between birth and the wrapping of the infant in warm blankets. After these fluctuations, a gradual return to normal occurs, and in health the temperature never varies far from this level. It is well established, however, that in adults the temperature of the body may vary from 1 to 1½ C. during each twenty-four hours. The maximum and minimum in the diurnal curve occur between 5 and 8 p. m. and 3 and 6 a. m., respectively. These fluctuations are probably the result of work and mode of living, but are not in casual relationship to the astronomical division of time.

The occurrence of an abnormal elevation of the infant's rectal temperature during the first week of life is seen with considerable frequency, and various theories have been advanced as to its cause. With the hope of adding additional information regarding this question, a study was undertaken at the Swedish hospital, Minneapolis.

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* Received for publication, Jan. 26, 1926.

1. Benedict and Talbot: Physiology of the Newborn, Washington, Carnegie Inst. Pub., No. 233, 1915.

ROUTINE OBSERVATIONS

The observations were taken from the hospital records of 817 full term infants delivered during 1921 and January, 1922. The routine observations included a daily record of the naked body weight, and a determination of the amount of milk obtained at each nursing at four hour intervals. In addition, the rectal temperature was taken every four hours during the first four days of life and once daily thereafter. In this study, the temperature was considered normal unless above 99.6 F.

The total number of full time living babies born during the period of study (817) is shown in table 1. Of these, 99 babies, or 12.2 per cent of the entire number, developed fever during the first week of life.

TABLE 1.—*Number of Living Babies Delivered Each Month, Number and Per Cent Having Fever; Totals and Also Average Per Cent*

	No. of Living Births	No. of Babies Having Fever	Per Cent
January 1921	49	4	8.2
February 1921	65	2	3.1
March 1921	55	0	0.0
April 1921	60	3	5.0
May 1921	69	12	17.4
June 1921	53	18	34.0
July 1921	65	18	27.7
August 1921	69	15	21.7
September 1921	65	15	23.1
October 1921	57	4	7.0
November 1921	62	4	6.5
December 1921	66	2	3.0
January 1922	82	2	2.4
Total	817	99	12.2

Inspection of the tables shows, however, that the percentage distribution of cases was by no means uniform throughout the year, varying from minimums of 0 to 2.4 per cent during March, 1921, and January, 1922, to maximums of 34.0 and 27.7 per cent during June and July, 1921, respectively. Of the 99 babies having fever during the thirteen month period of study, 87.8 per cent of the cases occurred from May to September, 1921, inclusive. This period, according to the U. S. weather bureau local records, was unusually warm, the maximum temperatures ranging from 91 to 99 F. Of the 321 babies born during these hot months, 24.3 per cent developed fever, the incidence being twice as large as during the entire thirteen months combined (12.2 per cent, table 1) and almost six times the incidence (4.3 per cent) occurring in the remaining eight months of the period of study. These findings suggest that high external temperatures of summer, especially those above the usual winter room temperature of 68 to 72 F., have a definite influence on the frequency of the occurrence of fever in new-born infants. The percentage of cases having an abnormal elevation of temperature for each month is shown graphically in chart 1. The

average duration of fever was 2.2 days, with a range of one to five days. In the majority of cases, the maximum fever occurred on the third and fourth days of life, with variations up to 105.2 F.

AVERAGE BIRTH WEIGHT

The average birth weight for the boys (table 2) was 3,584 Gm., which decreased to a minimum of 3,257 Gm. on the fourth day of life. The loss in weight amounted to 327 Gm., or 9.1 per cent of the initial weight. For the girls, the weight decreased from an average of 3,511 Gm. at birth to 3,105 Gm. on the fourth day, the loss (406 Gm.) amounting to

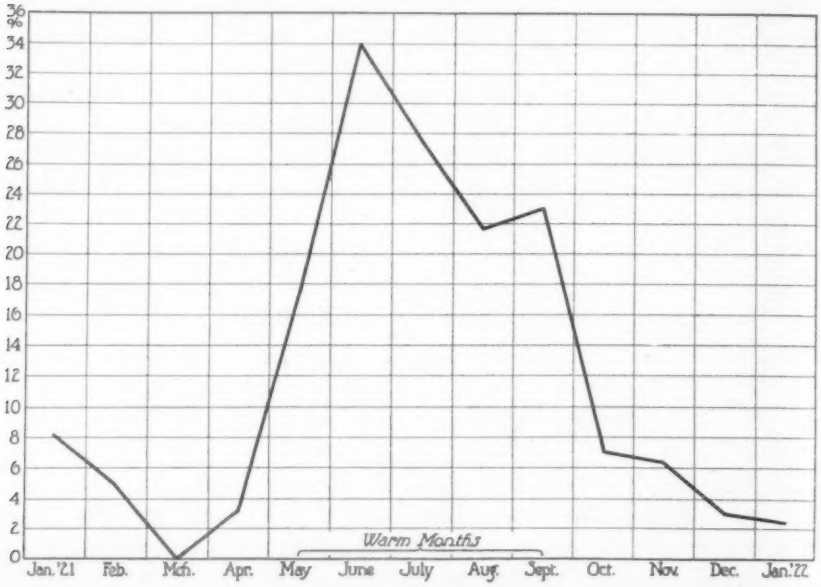

Chart showing a monthly percentage of babies having fever.

11.6 per cent of the birth weight. For the sexes combined, the loss in weight amounted approximately to 10.3 per cent.

From a study by Adair and Stewart,[2] the average loss of weight for 298 full term infants born at the same hospital (Swedish), and subject to the same routine as the present series, amounted to about 7.5 per cent of the birth weight, or about 2.5 per cent less than the loss registered for the babies having a fever during the new-born period. The greatest loss for each sex occurred on the third day in the present series of cases, whereas with the 1922 series the greatest loss was on the second day.

After the fourth day the gain in weight (table 2) was irregular, and by the tenth day the boys were 4.9, and the girls 6.2 per cent below

2. Adair, F. L., and Stewart, C. A.: Milk Ingestion in Relation to Changes in Body Weight of New-Born Infants, J. A. M. A. **78**:1865 (June 17) 1922.

the initial birth weight. In the 1922 series at the tenth day, the average weight was only 2.5 per cent below the birth weight. The weight changes of the babies having fever, therefore, show a greater loss and a slower return to normal than noted by Adair and Stewart for babies kept under identical conditions. That the smaller number of cases included in the present study may account in part at least for this difference cannot be denied.

TABLE 2.—*Number of Cases, Age and Weight (Sexes Separated), and Average Lactose and Breast Milk Ingestion Per Feeding (Sexes Combined)*

Boys			Girls			Sexes Combined	
No. of Cases	Age, Days	Weight, Gm.	No. of Cases	Age, Days	Weight, Gm.	10% Lactose Solution, Cc.	Breast Milk, Gm.
52	1	3,584	44	1	3,511	10.2	12.2
53	2	3,433	34	2	3,343	16.2	22.0
51	3	3,272	37	3	3,173	16.2	34.2
52	4	3,257	42	4	3,105	19.2	45.8
52	5	3,291	41	5	3,198	25.2	53.8
50	6	3,359	39	6	3,203	18.2	60.8
50	7	3,344	39	7	3,222	17.4	65.2
48	8	3,367	41	8	3,249	....	66.8
49	9	3,414	37	9	3,290	....	71.8
43	10	3,407	34	10	3,294	....	....

TOTAL INTAKE OF FOOD

The amount of 10 per cent lactose solution taken per feeding during the first few days (table 2, sexes combined) increased for an average of 10.2 cc. on the first day of life to 25.2 cc. on the fifth day. The following two days the lactose ingestion decreased, and none was taken after the seventh day. The quantity of breast milk obtained at each nursing increased from an average of 12.2 Gm. on the second day to 71.8 Gm. on the tenth day. The average total milk intake for the first ten days amounted to 2,163 Gm. In addition, these babies also took 613.0 cc. of the lactose solution making the total intake for the period 2,776 cc.

In the series reported by Adair and Stewart [2] during a similar period, the average total amount of breast milk obtained was 2,555.1 Gm., or 392.1 cc. more than that obtained by the babies with fever. The 1922 series also had an average total lactose solution intake of 549.5 cc., or 63.5 cc. less than that taken by the babies in the present group. The total fluid intake of the 1922 series (3,104.6 Gm.), as compared with the present series (2,776 Gm.), was 328.6 cc. greater in the former.

From reports in the literature, inanition fever is accompanied by many changes, particularly in the blood. Sherman, Pucher and Lohnes [3] report that in all febrile cases there is a pronounced increase of

3. Sherman, D. H.; Pucher, G. W., and Lohnes, H. R.: Blood Chemistry of the New-Born in Health and in Inanition Fever, Am. J. Dis. Child. **30**:496 (Oct.) 1925.

urea, nitrogen and amino-acid nitrogen, especially in those more severely ill. A diminished alkali reserve sufficient to produce a decided acidosis is also reported. Changes in the blood concentration also have been reported by Marriott [4] (1920-1921), Bakwin [5] and others. Bakwin reports that fluid given by mouth in proportions of 30 to 40 cc. per kilogram of body weight produces a prompt fall in temperature in the blood concentration. The temperature usually becomes normal in from 30 to 90 minutes after administration. Relief is obtained much more promptly when fluid is given by mouth than by intraperitoneal or subcutaneous injection.

COMMENT

From the present study, it appears that high external temperatures at least influence the incidence of fever among new-born babies. Additional factors apparently contributing to the condition are the subnormal fluid intake and excessive loss in weight, characteristic of babies having fever during the new-born period. The prompt subsidence of the fever on the liberal administration of fluids strongly suggests that dehydration is a very important causative factor.

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4. Marriott, W. M.: Some Phases of Pathology of Nutrition in Infancy, Am. J. Dis. Child. **20**:461 (Dec.) 1920.

5. Bakwin, H., and Goss, C.: Dehydration Fever in New-Borns, Am. J. Dis. Child. **24**:508-519 (Dec.) 1922.

THE PROPHYLAXIS OF VARICELLA WITH VESICLE FLUID*

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Vaccination of exposed patients with the contents of varicella vesicles is not new. In 1913 Kling [1] was quite successful with this procedure. It has also been used with more or less favorable results by Handrick,[2] Rabinoff,[3] Michael [4] and others. Lately, the use of convalescent varicella serum has been tried by Blackfan [5] and by Weech,[6] with satisfactory results. Hess and Unger [7] reported excellent results in varicella prophylaxis with vesicle fluid injected intravenously. Vaccination with vesicle fluid, using the same technic as with smallpox vaccination, would seem to be the simplest procedure, and it has this advantage over convalescent serum prophylaxis in that an active instead of a passive immunity is obtained. During the past two years, I have had the opportunity of testing the efficacy of varicella vesicle fluid in checking the spread of this disease, and the results have been so satisfactory that it has seemed of interest to report them with some experiments in animal inoculation.

TECHNIC

To secure the best results, vaccination should be performed on the first or second day of exposure. This was done in all cases. The contents of a fresh vesicle is drawn into a capillary tube (after cleansing the vesicle with alcohol and saline solution and wiping dry with cotton). The contents of the tube is expressed onto the forearm of the patient to be vaccinated, and forty or fifty punctures through this fluid are made with a sterile needle; the needle merely punctures the epidermis and no blood is obtained. The procedure is practically painless and can be done in a minute or two. The fluid is allowed to dry on the arm and seals the punctures. If a "take" occurs, it will be noticed that between the eighth and thirteenth day, a papule appears at the site of vaccination. This rapidly changes to a vesicle and then to a crust

* Received for publication, Feb. 9, 1925.

* From the isolation department, Milwaukee Children's Hospital.

1. Kling, C. A.: Berl. klin. Wchnschr. **50**:2083, 1913.
2. Handrick, E.: Monatschr. f. Kinderh. **13**:242, 1914.
3. Rabinoff, S.: Arch. Pediat. **32**:651, 1915.
4. Michael, M.: Arch. Pediat. **34**:702 (Sept.) 1917.
5. Blackfan, K. D.; Peterson, M. F., and Conroy, F. C.: Ohio State M. J. **19**:97 (Feb.) 1923.
6. Weech, A. A.: The Prophylaxis of Varicella with Convalescent's Serum, J. A. M. A. **82**:1245 (April 19) 1925.
7. Hess, A. F., and Unger, L. J.: A Protective Therapy for Varicella and a Consideration of its Pathogenesis, Am. J. Dis. Child. **16**:34 (July) 1918.

which later drops off, leaving in some instances a scar which resembles the scar remaining after smallpox vaccination. There is usually no fever nor discomfort from the vaccination. Precautions are taken to avoid the use of vesicle fluid from syphilitic patients.

VACCINATION EXPERIMENTS

Experiment 1.—This was made on May 13, 1924. On the first day of exposure from an active case, four children were vaccinated. The history in all was negative for varicella. Three children showed no "takes"; one child developed a papule on the twelfth day after vaccination, which became vesicular and which later crusted. After seven days, a slight scar remained. None of the children developed varicella. A patient convalescing from varicella was vaccinated at the same time, with negative results.

Experiment 2.—This was made on the same day as experiment 1. Six children with surgical tuberculosis were vaccinated on the day of exposure. There was but one "take" (L. P.), which ran the usual course. None of the children developed varicella. An interesting observation was made with the patient L. P., who was successfully vaccinated on May 13, 1924. This patient remained in the hospital, and on Jan. 8, 1926, contracted a moderately severe case of varicella. It was not known previous to the outbreak of the eruption that he had been exposed. Thus was seen for the first time the duration of the immunity produced by inoculation with vesicle fluid. In this particular case it was less than eighteen months. It is known, of course, that persons who have been vaccinated successfully against smallpox possibly may contract the disease two or three years later. The immunity induced by any vaccination is never complete, and may be broken down in the presence of overwhelming infection. Conclusions cannot be drawn from one case, but it suggests that the immunity induced by vaccination with the vesicle fluid of varicella is of shorter duration than in vaccination with variola fluid. This conjecture agrees with the fact that it is more difficult to secure "takes" with varicella than with variola vaccination.

Experiment 3.—This was made on June 9, 1924. Seven patients exposed to varicella were vaccinated with vesicle fluid, taken from a child exposed at home two weeks before admission. The patients were vaccinated on the second day after exposure. There were three "takes," three children did not "take" and one child left the hospital before the eighth day. None of the children developed varicella.

Experiment 4.—This was made on the same day as experiment 3. Four patients were vaccinated with vesicle fluid from a patient with varicella (exposed at home) on the first day of their exposure. Two patients obtained "takes" and two were negative. One of the patients

with a positive reaction (C. K.) had an elevation of temperature to 101 F. on the ninth day after vaccination, which lasted for two days. His arm showed an active reaction; on his face and chest about ten macules but no vesicles developed, and the macules disappeared after three days. This was either a case of varicella aborted by vaccination, or more probably a severe reaction to the inoculation. The three remaining patients did not develop varicella.

Experiment 5.—This was made on July 24, 1924. Seven children were vaccinated on the third day of exposure. There were four "takes" and three negative reactions. One child (S. K.) who had been vaccinated successfully six weeks before was also exposed but was not revaccinated. None of these children contracted varicella. One of the children had fever and headache at the time of the reaction.

Experiment 6.—This was made on July 26. One child was vaccinated on the day of exposure and a "take" was obtained. She did not contract varicella.

Experiment 7.—This was made on Jan. 13, 1925. One child was vaccinated on the day of exposure, with no subsequent reaction; he did not contract varicella.

Experiment 8.—This was made on May 8, 1925. Five nurses who had never contracted varicella were vaccinated on the second day of exposure. Five "takes" were obtained, and no subject developed varicella.

Experiment 9.—This was made on July 8. Three children were vaccinated on the day of exposure. Two "takes" and one negative reaction were obtained; no case of varicella developed.

SUMMARY

Thirty-six persons were vaccinated against varicella. There were nineteen "takes," sixteen negative reactions, and one patient who left the hospital before the eighth day. No cases of varicella developed in those inoculated either successfully or unsuccessfully, unless the one child mentioned in experiment 4 is regarded as an abortive case of varicella. It is impossible to be sure that all of these patients had never contracted varicella at a previous time, because a history is often unreliable. Some of these patients who gave a negative reaction may have had varicella before. There were seven patients serving as involuntary controls during these experiments who developed varicella. They were not vaccinated because it was not known that they had been exposed. The chief obstacle to checking the spread of varicella in the hospital is the fact that it is difficult to know who has been exposed. On one floor of a building a child may develop varicella and later a child on another floor may contract the disease. In some instances, it

appears that the disease must be carried by a third person. The results of these experiments show that vaccination against varicella is effective. It is also shown that one child reexposed to varicella eighteen months after successful vaccination contracted the disease. Another child reexposed six weeks after a successful vaccination did not contract the disease. The use of the contents of the varicella vesicles for vaccination would seem to be the simplest method of checking an epidemic.

EXPERIMENTS WITH VARICELLA CRUSTS

An attempt was made to prepare a varicella vaccine, using the crusts taken from convalescent patients. A number of crusts were collected and macerated thoroughly in a solution of equal parts of glycerin and water. The preparation was kept in the icebox and was mixed thoroughly every day.

Experiment 1.—(Crust fluid five days after preparation.) Three children, whose history was negative for varicella, were vaccinated with the crust fluid. Each child received three scarifications with a Pirquet chisel and a large quantity of the fluid was rubbed in thoroughly. No evidence of any reaction occurred.

Experiment 2.—(Crust fluid twenty-two days after preparation). Six children were vaccinated with the varicella crust fluid, using the needle puncture method. Their history was negative for varicella. No reaction was visible during the twenty-two days the patients were under observation. One of these children (S. K.) was later vaccinated with vesicle fluid, and a positive reaction was obtained. The results of these two experiments would indicate that varicella crusts are inert. Further work along this line is contemplated.

ANIMAL INOCULATIONS

In the past, numerous attempts to transmit varicella to animals have always ended in failure. The recent work of Teague and Goodpasture [8] with herpes zoster, using coal tar as a preliminary epithelial stimulant, suggested a repetition of their work with the virus of varicella. After the skin had been rendered susceptible with previous coal tar applications, Teague and Goodpasture were able to inoculate guinea-pigs with herpes virus quite easily. The results of experiments on four guinea-pigs were negative. At four day intervals the animals received two applications of coal tar, after first shaving the skin. Each pig received several inoculations, using crust fluid, vesicle fluid and vesicle fluid from vaccinated patients. Injections were made with the needle puncture method, scratch method and the intradermal method. In no case was

8. Teague, O., and Goodpasture, E. W.: Experimental Herpes Zoster. J. A. M. A. **81**:377 (April 4) 1923.

any reaction visible during a month of observation. These experiments are too few to be absolutely conclusive, but they agree with the results of previous workers.

ADDITIONAL OBSERVATIONS

A few children who had received considerable quartz light therapy and later contracted varicella were observed. The eruption in all cases was fairly profuse. The lesions seemed to involute more quickly than in other children.

In view of the recent work of Netter and Urbain,[9] expressing their belief that herpes zoster and varicella are closely related if not identical, it is interesting to note that I developed a mild case of herpes zoster while working with the varicella virus. I had contracted varicella in childhood. This may have been merely a coincidence, but is worthy of note. There are many workers who disagree with the views of Netter and Urbain.

CONCLUSIONS

1. Varicella prophylaxis, using varicella vesicle fluid with the needle puncture method, is successful in checking the spread of the disease.

2. The duration of the immunity induced by this procedure was less than eighteen months in one instance and more than six weeks in another.

3. The use of varicella crusts to produce vaccine was not successful in the few instances when it was tried.

4. Inoculation of guinea-pigs with varicella virus, using the coal tar method of Teague and Goodpasture, was unsuccessful.

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9. Netter, A., and Urbain, A.: Compt. rend. Soc. de biol. **90**:461 (Feb.) 1924.

THE KIDNEY: A FILTER FOR BACTERIA

VII. THE PASSAGE OF BACILLUS COLI THROUGH THE KIDNEY WITH ACUTE STAPHYLOCOCCIC LESIONS *

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The difficulties encountered in previous experiments in trying to effect a rapid passage of bacteria through the normal kidney led us to investigate the permeability of an acutely infected kidney. The frequency with which pyelitis occurs secondary to infections in other parts of the body, as well as the relationship of focal infection to pyelitis, as demonstrated by Bumpus and Meisser,[1] and Haden,[2] makes it seem probable that the invasion of the colon bacillus is often only secondary to some acute lesion of the kidney. Once established, the colon bacillus maintains the infection which would otherwise have subsided with the disappearance of the primary infection. That the colon bacillus is frequently the primary infecting agent and usually the secondary invader is generally accepted, but by what route it reaches the kidney has never been proved.

It has been taken for granted, since the colon bacillus may find its way into the circulation, that its entrance into the urinary passages is by way of the blood stream. That the colon bacillus enters the circulation in any great numbers from the intestine, except as the result of complete obstruction, is very unlikely in view of the recent researches of David and McGill.[3] Furthermore, in cases of septic infection of the uterus associated with colon bacillus septicemia, colon bacilli are not constantly found in the urine. In twenty-six of forty cases, with blood cultures positive for colon bacillus, Levy [4] found sterile urine on culture. Also, our work on the kidney as a filter for bacteria would tend to prove that bacteria are not excreted immediately when large numbers of

* Received for publication, Feb. 11, 1926.

* From the Section on Pediatrics, Mayo Clinic.

1. Bumpus, H. C., Jr., and Meisser, J. G.: Foci of Infection in Cases of Pyelonephritis, Study II. J. A. M. A. **77**:1475-1479 (Nov. 5) 1921; Focal Infection and Selective Localization of Streptococci in Pyelonephritis, Arch. Int. Med. **27**:326-337 (March) 1921.

2. Haden, R. L.: The Relation of Chronic Foci of Infection to Kidney Infection, Am. J. M. Sc. **169**:407-419 (March) 1925.

3. David, V. C., and McGill, E. C.: Relation of the Bowel to B. coli Kidney Infections, J. Urol. **10**:233-254 (Sept.) 1923.

4. Levy, Alfred: Kritische Studie über die Infektionswege bei Pyelitis acuta auf Grund klinischer Beobachtungen, Deutsch. Arch. f. klin. Med. **138**:1-17, 1921.

them circulate through the kidney.[5] The question of the ascending route must be left open, as we have no experimental evidence regarding it. We are concerned in this study with the effect of an acute lesion of the kidney on its permeability for colon bacilli introduced into the circulation.

TECHNIC

The animals were injected intravenously with a twenty-four hour culture of staphylococcus, after a preliminary catheterization to determine that the urine was sterile. From two to eight days later, when the urine showed many staphylococci and large amounts of pus, a twenty-four hour culture of colon bacillus was injected intravenously. The animals were killed by chloroform at varying intervals after the injection, and the urine was examined for colon bacilli. In four short-interval experiments, sucrose diuresis was used, and a count was made of the number of colonies of staphylococci to each cubic centimeter and the presence of colon bacilli tested for, at hourly intervals up to four hours. In the longer experiments, catheterized specimens were taken after three, six and twenty-four hours, and longer.

The cultures were made in litmus lactose agar in the diuresis experiments, but in all the others the urine was first treated with gentian violet so as to kill off the staphylococci, and then added to the broth in the usual way. In this way, even small numbers of colon bacilli could be found with an overwhelming number of staphylococci. Colon bacilli added as controls to the urine containing staphylococci were found without difficulty in the urine treated with gentian violet.

EXPERIMENTS WITH DIURESIS

As will be seen from table 1, injections of sucrose were made in rabbits that had had staphylococcus injections from two to eight days before. There were large amounts of pus in the urine at the time of the colon bacillus injections and abscesses were found in the kidneys at necropsy. One animal received 220 cc. of 10 per cent sucrose, the second 237 cc., the third 160 cc. and the fourth 320 cc. in the four hours. At the start of the experiment, all four rabbits had innumerable bacteria and countless pus cells in the urine. At the end of one hour the condition was about the same. At the end of the second, third and fourth hours, the pus had progressively diminished and the number of bacteria was greatly reduced.

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5. Helmholz, H. F., and Millikin, Frances: The Kidney: A Filter for Bacteria. I. The Presence of Bacteria in Blood, Kidney and Urine After Varying Intervals Following Intravenous Injection, Am. J. Dis. Child. **29**:497-505 (April) 1925.

In rabbit A 15, at the end of the first hour, there were innumerable organisms in 1 cc. of urine. At the end of the second hour, there were 300 colonies in 1 cc., and at the end of the fourth hour, 100 colonies in 1 cc. Two animals died a few hours after the end of the experiment and two were found dead the following day. On culture of the blood and urine, one animal had a growth of colon bacillus and the other had colon

TABLE 1.—*The Effect of Diuresis Produced by Sucrose on the Passage of Colon Bacilli Through an Abscessed Kidney*

Rabbit	Days Between Injection of Staphylococcus and Bacillus coli	Degree of Pus in Urine	20 per Cent Sucrose Injected	Urine Specimens	Staphylococcus in Blood	Staphylococcus in Urine	Colon Bacillus in Blood	Colon Bacillus in Urine	Remarks
754	8	1st hr. 4	220 cc. for four hours	Catheterized after 1 hr.	..	+	..	—	Abscesses; 200 cc. urine passed during experiment
		2d hr. 4		Catheterized after 2 hr.	..	+	..	—	
		3d hr. 1		Catheterized after 3 hr.	..	+	..	—	
		4th hr. 1		Catheterized after 4 hr.	..	+	..	—	
				Taken at death, 1 day later	—	—	+	+	
755	8	1st hr. 4	237 cc. for four hours	Catheterized after 1 hr.	..	+	..	—	Abscesses; 200 cc. urine passed during experiment
		2d hr. 2		Catheterized after 2 hr.	..	+	..	—	
		3d hr. 1		Catheterized after 3 hr.	..	+	..	—	
		4th hr. 1		Catheterized after 4 hr.	..	+	..	—	
				Taken at death, 1 day later	—	+	+	—	
A13	3	1st hr. 3	100 cc.	Catheterized after 1 hr.	..	+	..	—	Abscesses; 210 cc. urine passed during experiment; 30 cc. in bladder at necropsy; colonies of staphylococcus in urine decreased in number each succeeding hr.
		2d hr. 2	36 cc.	Catheterized after 2 hr.	..	+	..	—	
		3d hr. 1	14 cc.	Catheterized after 3 hr	..	+	..	—	
		4th hr. 0	10 cc.	Catheterized after 4 hr.	..	+	..	—	
				Taken at death, 7.5 hr. later	—	+	+	—	
A15	2	1st hr. 4	100 cc.	Catheterized after 1 hr.	..	+	..	—	Abscesses in kidney medulla; no urine in bladder at end of experiment
		2d hr. 1	65 cc.	Catheterized after 2 hr.	..	+	..	—	
		3d hr. 0	85 cc.	Catheterized after 3 hr.	..	—	..	—	
		4th hr. 0	70 cc.	Catheterized after 4 hr.	..	+	..	—	
				Taken at death, 4.5 hr. later	—	..	+	..	

bacillus in the blood and staphylococcus in pure culture from the urine. In none of the cultures taken one, two, three, or four hours after injection were any colon bacilli grown from the urine.

EXPERIMENTS WITHOUT DIURESIS

The first series comprises sixteen experiments extending over periods of from one and a half hours to two weeks, although one experiment was carried along for forty-nine days to determine the character of

the staphylococci lesions rather than the presence of the colon bacillus. Pus 4 was present in all the specimens of urine examined before the injection of the colon bacillus, and at necropsy abscesses were found in the kidneys of all animals.

As will be seen from table 2, there is a surprising uniformity in the results. Colon bacilli were almost constantly present in the blood, but not in the urine. Staphylococci only were found in the urine. In only two experiments (936 and 930), in which the animals died after five and nine days respectively, were colon bacilli found in the urine. These two animals were not killed but died some hours before necropsy was performed and the urine cultured. After such an interval, it is not unusual to find colon bacilli in the urine even when no organisms have

TABLE 2.—*Impermeability for Colon Bacilli of the Kidney Injected with Staphylococcus*

Rabbit	Days Between Injection of Staphylococcus and B. coli	Degree of Pus in Urine at Injection of B. coli	Time Between Injection of B. coli and Examination of Urine for Bacteria	Staphylococcus in		Bacillus coli in		Remarks
				Blood	Urine	Blood	Urine	
817	2	4	1.5 hours	—	—	+	—	
764	2	4	2 hours	—	+	+	—	Abscesses
806	2	4	2 hours	—	+	+	—	
805	2	4	5 hours	—	+	+	—	
821	1	...	7 hours	..	+	..	—	Abscesses
766	2	4	8.25 hours	—	—	+	—	Abscesses
767	2	4	8.5 hours	—	+	—	—	
989	3	4	1 hour	—	—	+	—	
986	2	4	3 hours	..	+	..	—	
			6 hours	..	+	..	—	
			1 day	..	+	+	—	Abscesses
987	2	4	3 hours	..	+	..	—	
			6 hours	..	+	..	—	
			1 day	..	+	+	—	Abscesses
990	3	4	2 days	..	..	—	—	Abscesses
			3 days	—	+	—	—	Abscesses
936	2	4	5 days	—	+	+	+	Abscesses
930	2	4	9 days	—	+	+	+	Abscesses
937	2	4	13 days	—	+	—	—	Abscesses
819	1	...	14 days	—	+	..	—	
820	1	...	49 days	..	—	..	—	Abscesses

been injected, so that the possibility of contamination after death had to be seriously considered.

The second series comprises twelve experiments on twelve rabbits in which the urine was tested repeatedly for the colon bacillus. The technic was practically the same as that used in the first series, except that the urine was obtained from the bladder by catheter instead of through the wall of the bladder at necropsy. It was thought at first that the urine in the bladder might be contaminated by inserting the catheter, but in only one instance was the colon bacillus found at a second examination when it was not present at the first. In only three of the twelve experiments (table 3) did the colon bacillus come through into the urine. In the first experiment it was found on the second day and also on the eleventh and twenty-second days; in the second, colon bacilli

were absent on the first day, but present on the fourth and seventh days, and in the third, the colon bacilli were present on the first and third days.

A third series of eleven experiments was then performed, in which staphylococci and colon bacilli were simultaneously injected into the ear vein in the rabbits. Staphylococci appeared in the urine in each of the experiments at the first examination, with one exception. In this case they were present on the third day and absent on the second. Abscesses in the kidney were found in all of the animals at necropsy.

In striking contrast to the constant presence of staphylococci is the appearance of colon bacilli in the urine in only three of the eleven experiments. In one experiment they were absent on the first day but

TABLE 3.—*The Appearance of Bacillus Coli in the Urine from a Kidney with Staphylococcic Lesions*

Rabbit	Days Between Injection of Staphylococcus and B. coli	Pus in Urine	Staphylococcus in Urine, Final Culture	Presence or Absence of B. coli in Urine: 1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	Presence or Absence of B. coli on Culture of Urine
A233	4	1	—	..	—	..	..	—	..	..	
A266	16	2	+	..	—	..	—	..	..	..	
A269	3	4	+	..	—	..	—	..	..	..	
A285	4	1	+	..	..	..	..	..	—	..	Negative on tenth and twelfth days
A312	3	1	..	..	+	..	..	..	..	..	Positive on eleventh and twenty-second days
A313	3	0	—	..	..	—	—	..	..	—	Negative twenty-one days after injection
A315	4	1	..	—	..	..	..	..	..	—	
A317*	4	1	+	—	..	..	+	..	..	+	
A324	3	1	+	—	..	—	..	..	..	..	
A325	3	4	+	—	..	—	..	—	..	..	
A326	3	4	+	—	..	..	..	..	..	..	
A327	3	1	+	+	..	+	..	..	..	..	

* Necropsy showed Bacillus coli and staphylococcus on culture of urine.

present on the second, twelfth, and twenty-fifth days. In another they were present on the second, fourth, and twenty-fifth days; in the third the urine was positive for the colon bacillus on the fourth, sixth, and forty-seventh days. The remainder of the experiments showed the urine free from colon bacilli for periods up to twenty-three days (table 4).

Repeated injections of colon bacilli were not tried because it seemed improbable that the colon bacilli would ever attain such numbers in the circulation or persist longer than they had in these experiments.

COMMENT

The presence of acute staphylococcic lesions of the renal parenchyma and pelvis does not render the kidney permeable to the colon bacillus for periods up to twenty-four hours, as was demonstrated by numerous experiments. Individual experiments in which the interval was

forty-eight hours, seventy-two hours, and more, up to three weeks, gave mostly negative results. As the two animals in series 1 that died after five and nine days, respectively, were examined some hours after death, the presence of colon bacilli in the urine from the bladder may have been due to contamination after death.

The four-hour experiments with diuresis produced by sucrose showed, in every instance, marked reduction in the pus and bacterial counts of the urine, which demonstrates the value of large amounts of fluid in washing out the urinary tract. In four hours urine that, at the beginning of the experiment, contained innumerable bacilli in 1 cc. was so diluted that it contained only 100 or less colonies to each cubic centimeter. Sucrose administered intravenously might therefore be of

TABLE 4.—*The Appearance of Bacteria in the Urine After Simultaneous Intravenous Injection of Staphylococcus and Bacillus Coli*

Rabbit	Presence or Absence of Staphylococcus in Urine (Days)							Presence or Absence of Bacillus coli in Urine (Days)							Presence or Absence of Bacillus coli on Culture of Urine
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	
A294	..	+	..	+	..	..	..	..	+	..	+	..	..	..	Positive on ninth and twenty-fifth days
A295	..	..	..	+	..	+	..	..	..	..	+	..	+	..	Positive on forty-seventh day
A301	+	..	..	+	..	..	..	—	..	..	—	..	..	..	Negative on eleventh, fourteenth, eighteenth and thirty-sixth days
A311	+	+	..	..	..	..	..	—	+	..	..	..	..	..	Positive on twelfth and twenty-fifth days
A314	+	+	+	..	+	..	+	—	—	—	..	—	—	—	
A328	..	+	+	..	..	..	..	..	—	—	..	..	..	—	Negative on eleventh day
A329	..	+	+	..	..	..	..	..	—	—	..	..	..	..	Negative on tenth and eleventh days
A330	..	—	+	..	..	..	..	..	—	—	..	..	..	—	Negative on tenth, eleventh and twenty-third days
A334	..	..	..	+	..	..	..	..	..	..	—	..	..	—	
A335	..	..	..	+	..	..	+	..	..	..	—	..	..	..	Negative on eighth and fifteenth days
A333	..	+	..	+	..	..	..	..	—	..	—	..	..	..	

great value in cases of pyelitis of infancy associated with temporary plugging of a ureter, and also in cases of extreme toxemia in which nausea and vomiting have prohibited the ingestion of large amounts of fluid. The effect of the diuresis in the experiments was only temporary, as in each instance the bacteria and pus cells were innumerable when the urine was examined the following morning.

The shorter experiments prove beyond doubt that the presence of an acute lesion in the renal tissue and in the pelvis of the rabbit does not make possible a rapid passage of colon bacilli from the blood into the urine. The results in longer experiments, twelve, twenty-four, forty-eight hours and more, indicate that, aside from the holding back of the colon bacilli by the kidney, the acute local lesions do not represent an area of lowered resistance when the colon bacillus can get a foothold and

develop a focus that would constantly feed infection to the urine. No histologic changes in the parenchyma or pelvis of the kidney were found that differed in any way from those produced by injection of the staphylococcus alone.

The bearing of these experiments on the problem of pyelitis in human beings seems quite definite, since the results add further evidence to that already at hand against the assumption that the secondary invasion of the pelvis by colon bacilli is through the blood stream. Streptococcic lesions of the kidney, as experimentally produced by Bumpus and Meisser, and Haden, in the rabbit, may have their counterpart in the lesions of man; but the colon bacillus does not necessarily enter the pelvis through the blood, as does the streptococcus. The fact that our urinary cultures were negative after large numbers of virulent colon bacilli had been introduced into the blood stream, and had circulated through the kidney, is definite proof of their failure to localize in the presence of local lesions. It can be assumed that the particular strain injected into the animals had no special affinity for the kidney, but one would then have to assume that in every case of pyelitis in human beings there was, in the intestinal canal or elsewhere in the body, a colon bacillus with specific affinity for the kidney.

It would be hazardous to attempt to draw any definite conclusions from this study, but evidence is brought forward which tends to show that staphylococcic lesions in the kidney do not predispose to secondary invasion of the urinary tract by the colon bacillus when intravenously injected.

SUMMARY

The presence of staphylococcic lesions of the renal parenchyma and pelvis does not predispose to the rapid passage of colon bacilli into the urine. Active diuresis produced by sucrose does not force bacteria through the infected kidney in less than four hours. The colon bacillus introduced intravenously does not tend to become a secondary invader in the urinary tract in the presence of staphylococcic lesions of the kidney in the rabbit. Staphylococci and colon bacilli introduced simultaneously into the vein of a rabbit do not appear simultaneously in the urine.

PROGRESS IN PEDIATRICS

DISEASES OF THE GENITO-URINARY TRACT IN CHILDREN

A REVIEW OF THE LITERATURE FROM JANUARY, 1925, TO JANUARY, 1926 *

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VULVOVAGINITIS IN CHILDREN

Fraser [1] gives an exhaustive discussion and bibliography of vulvovaginitis in children. In a review of the literature on modes of infection, he calls attention especially to the work of Engering, who showed that the viability of the gonococcus outside the human body is greater than has generally been supposed. He found that the gonococci lived from three to ten hours in sterile tap water at a temperature of 22 C., and in the surface water of swimming pools from seven and a half to ten hours. The gonococci remained alive on moist linen for four hours. He also emphasizes the importance of investigating the adult members of the household. Many other organisms may be the etiologic factor in vulvovaginitis, but usually, however, they are secondary to an original gonococcal infection. Uncleanliness and the immaturity of the vulva and vagina are important predisposing factors. Fraser states that vulvitis is the main symptom of the disease; he believes that it seldom extends beyond the lower third of the vagina. It rapidly progresses to a stage of chronicity with only slight nonpurulent discharge, but gonococci can be recovered in cultures from secretions which are negative in smears. The disease runs a long course with frequent relapses. There is involvement of the rectum in the vast majority of cases, and this is frequently a source of reinfection. Metastatic or direct extension complications are rare.

Most authors believe the disease does not persist into adult life. Epstein states that he has had the condition persisting in children from infancy until the age of 10. Wessels suggests that these chronic inflammations in childhood are important etiologic factors of so-called congenital anomalies. There is great difficulty in the demonstration of the gonococcus in discharge in chronic cases, but he believes that with the exception of the few cases due to the pneumococcus they are primarily a gonococcal infection. Frequently, positive cultures may be demonstrated from the rectum when vulval and urethral cultures are

* Received for publication, May 12, 1926.

1. Fraser, A. R.: Venereal Disease Information **7**:1-23 (Jan.) 1926.

negative. Fraser believes that the sequelae of vulvovaginitis are more important than the complications. He divides these into two groups, namely, the evolution of the carrier and the accomplishment of anatomic damage. Special instruments are necessary for the proper examination of the patient, such as speculums or urethroscopes. Provocative reactions sometimes are of value on the day previous to the bacteriologic examination. He details the important factors in prophylaxis and reviews the literature on treatment. In addition to the local treatment, Fraser advocates the use of vaccines in the treatment of vulvovaginitis, but stresses the importance of giving the proper dosage. He also advocates the use of colloidal manganese and, finally, he outlines a very rigid standard of cure.

McKelvey and his co-workers [2] discuss the different phases of gonorrhea in female children, as suggested by the study of fifty-two cases during a period of five years. As sources of infection they state that the disease may be contracted occasionally by passage through the birth canal in breech presentations, and by precocious sexual intercourse. They also emphasize the frequency of infection from older members of the family. They recognize the extreme susceptibility to gonorrheal infections because of the absence of squamous epithelium in the vagina of young girls and infants. The spontaneous cure at the time of puberty is largely due to a tissue development. They emphasize the importance of extreme precautions to prevent direct or indirect infection from the adult members of the family. It is difficult to tell when the patient is cured of gonorrhea, and recurrences are quite frequent.

Bloomberg and Barenberg [3] found gram-negative intracellular diplococci in the smears from the rectum of every child in a series of forty-one cases, in which the striking symptom was bloody stools. Dysentery bacilli were not found in the cultures; there was usually an associated vaginitis.

According to Byfield and Floyd,[4] gonorrheal infection of the rectum in infants through the medium of the rectal thermometer, may be an unsuspected source of epidemics of vulvovaginitis. Rectum infection often produces such slight symptoms that it is frequently overlooked.

PYELITIS

Sauer [5] states that neonatal pyelitis occurs more frequently in male infants. In the clinical picture, gastro-intestinal symptoms, especially

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2. McKelvey, S. R.; Muney, N., and Dunklee, G. K.: Venereal Disease Information **6**:289-296 (Oct. 20) 1925.

3. Bloomberg, M. W., and Barenberg, L. H.: Gonorrheal Proctitis as a Cause of Blood and Mucus in the Stools of Infants, Am. J. Dis. Child. **29**:206 (Feb.) 1925.

4. Byfield, A. H., and Floyd, M. L.: Arch. Pediat. **41**:673, 1924.

5. Sauer, I. W.: Neonatal Pyelitis, J. A. M. A. **85**:327-329 (Aug. 1) 1925.

vomiting, anorexia, diarrhea and tympanites predominate. He found pus and *B. coli* in the urine of fourteen out of fifteen nonthriving new-born infants with gastro-intestinal symptoms. Within six weeks, the disease usually responded to continued alkalinization of the urine. He believes that the infection occurs through the blood stream.

Dowler [6] stresses the importance of miscroscopic examination of the urine in any recurring fever of obscure origin, since pyelitis is the most common cause in the absence of physical findings. He favors the alkalinization treatment.

Pyelitis in the new-born infant, which has generally been considered an uncommon disease, was found in six patients by Graham.[7] He considers it the result of lowered resistance and he found the causative organism to be *B. coli,* nonhemolytic streptococcus and *Staphylococcus aureus* of two cases respectively. Since the onset occurred about the second or the third day, he considers the possibility of an intra-uterine infection or infection at the time of birth. He had good results from the use of alkaline medication.

Hodge [8] emphasizes the importance of recognizing the relation of a primary focus of infection in the tonsil to staphylococcal pyelitis and pyelonephritis of early childhood, since the successful result depends on the eradication of the foci.

Sickenga [9] found that a bacteriophage was constant in four cases of colon bacillus pyelitis in children, aged from 5 weeks to 3½ years. In twelve others, a bacteriophage was found occasionally, while in ten it was not found at all. The course of the disease did not seem to be influenced by the presence or absence of the bacteriophage. Vaccines did not change the bacteriophage findings, but the presence of the bacteriophage seemed to detract from the action of the vaccine. Sodium citrate proved to be the most efficient drug.

NEPHRITIS

Schlutz [10] believes that nephritis in infancy and childhood differs from that in the adult because of constitutional factors such as a better cardiovascular system in the young, and because of less likelihood of weakening by the presence of other disease conditions. Acute hemorrhagic nephritis is common in children, but the cardiorenal type is rare. The four more common types seen in childhood are: Acute hemorrhagic nephritis, acute exudative tubular nephritis or nephrosis type, chronic so-called "pedonephritis" of Heubner and the more severe

6. Dowler, V. B.: Canad. M. A. J. **15**:41-44 (Jan.) 1925.
7. Graham, R. H.: Am. J. M. Sc. **70**:401-404 (Sept.) 1925.
8. Hodge, E. H. Vere: Indian M. Gaz. **60**:459-460 (Oct.) 1925.
9. Sickenga, F. N.: Nederl. Maandschr. v. Geneesk. **13**:141-247, 1925.
10. Schlutz, F. W.: Minnesota Med. **7**:761-765 (Dec.) 1924.

chronic nephritis with contracted kidney and hypertension. The condition usually begins suddenly, with edema (often the earliest symptom) which is persistent, and frequently recurs after slight remissions. The amount of edema indicates the severity of the disease. Complete recovery of the function of the kidney usually occurs in the mild type. In severe cases, the course simulates more closely the course of the adult parenchymatous type. The two important principles in the treatment are the prevention of waste product accumulation in the blood and tissues, and the sparing of the kidney as much as possible. The protein and salt content in the diet are the two important factors; the salt should be restricted in all subjects with edema, and a low protein diet is a safe rule but is not necessary in all types. As a rule, drugs are of little aid except the use of theobromine sodiosalicylate in the nephrosis type. It is important to recognize and eradicate any focal infections about the throat, accessory sinuses and teeth. Most patients recover entirely in from six to twelve weeks, and the kidneys apparently can recover their function entirely. An attack of nephritis in childhood does not seem to influence the development of the condition in adult life.

Logue [11] classifies nephritis according to the clinical picture, the duration of the disease and the prognosis. Group 1, or nephrosis, he believes is theoretically due to a toxemia of the body cells by products of decomposition of diseased tubular epithelium. There is a reduced excretion of sodium chloride and water during the stage of edema, and a tendency to eclamptic uremia. The nitrogen excretion is normal or increased. Prognosis must be guarded in this type, as there is transition to contracted kidney or recovery. Group 2, or acute diffuse glomerular nephropathies, is associated with the infectious diseases, particularly scarlet fever. It is characterized by a marked reduction in the excretion of nitrogen waste products in the urine, and a corresponding increase of the retention products in the blood and tissues. Group 3, or pedonephritis (Heubner), extends over months or years, with an occasional acute stage but without outward signs such as edema, hematuria or high blood pressure. Group 4, or contracted kidney, is nephritis with a high blood pressure and has a similar course to that in the adult.

Allison [12] studied twelve acute cases; only two patients gave a family history of nephritis. There were enlarged tonsils and adenoids in eight, otitis media in two, and no evidence of focus infection in the other two. The onset was insidious in all, with a duration of from two to twelve weeks. He considers the removal of the focus of infection a most important part of the treatment and thinks this should be done after the acute stage of the disease has subsided, except in those cases

11. Logue, J. A.: Atlantic M. J. **28**:564-568 (June) 1925.
12. Allison, R. S.: Practitioner **114**:222-223 (March) 1925.

in which there are exacerbations and then the operation should not be delayed. Examination of the children nine months to one year afterward showed no trace of the disease.

Clausen [13] emphasized the importance of recognizing that infection of the paranasal sinuses is an etiologic factor in parenchymatous nephritis. Renal lesions are confined to the kidney tubules. He believes that the kidney disease is only a part of the infection of the whole body with a decreased resistance to infections of all sorts. *Staphylococcus aureus* or *S. albus* were most frequently obtained from the sinuses. An acute streptococcic infection can usually be found in acute hemorrhagic nephritis.

Schiff and Bayer [14] concluded that by limiting the ingestion of water in infants, there occurred a slight albuminuria with the presence of leukocytes, cylinders and erythrocytes in the sediment. This syndrome is dependent on the deficiency of water and is not related to the quality of the nourishment. It corresponds to the picture of pyuria, and clinically is the same in dehydrations of different intensities and etiologies. Infections may be followed by a dehydration pyuria, which is a kidney injury with decreased resistance. This predisposes to renal abscesses when a bacteriemia occurs. The colon bacilli can seldom be considered the exciting cause of pyuria in the infant.

Kohn [15] states that there is a marked nitrogen retention in nephritis with hypertension. In other conditions there is moderate or no nitrogen retention. The inorganic constituents of the blood, such as calcium potassium, sodium and phosphorus remain fairly normal and constant even through the stages from normal to marked edema.

Ebel [16] states that large doses of urea may be effective, when all other diuretics have failed in nephritis of the nephrosis type.

MISCELLANEOUS

Falci [17] gives a comparison of renal tuberculosis in children and in adults. The disease is rare in young children, but both kidneys are involved twice as often as in adults and the bilateral infection is rapidly fatal in children. The proportion rapidly increases with age, becoming most frequent between 12 and 18. The recovery following operation in unilateral tuberculosis is lower than in adults. The course of the bilateral disease progresses more rapidly in children than in adults.

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13. Clausen, S. W.: Parenchymatous Nephritis, Am. J. Dis. Child. **29**:587-593 (May) 1925.
14. Schiff, E., and Bayer, W.: Jahrb. f. Kinderh. **108**:157-170 (April) 1925.
15. Kohn, J. T.: Inorganic Constituents of the Blood in Nephritis of Children, Am. J. Dis. Child. **30**:40-42 (July) 1925.
16. Ebel: Monatschr. f. Kinderh. **29**:97-192 (Nov.) 1924.
17. Falci, E.: J. d'urol. **20**:273-352 (Oct.) 1925.

Scholl and his co-workers [18] state that prostatic tumors in childhood occur rarely. The various types of sarcomas found by Sysak in twenty-two cases compiled from the literature are classified.

Lyman [19] gives a report of his case, and a general discussion of this type of tumor in general. He considers trauma as an etiologic factor in stimulating the proliferation of aberrant cells in the kidney, with perhaps some inherited cancerous diathesis. In England, between 1901 and 1911, inclusive, the fatalities from cancer of the kidney and suprarenal capsule in children under 15 years, were 430 in those under 5 years, and 127 in those between 5 and 15 years. There is practically always metastasis into the lungs, vena cava, renal vein, lymph glands, liver or the other kidney. The average duration is eight months. It is frequently symptomless in the early stage, with or without hematuria. The predominant late symptoms are those of pressure, such as constipation, diarrhea, jaundice, edema, ascites, cough, cachexia and emaciation. Radiotherapy may diminish the size of the tumor. This condition always terminates fatally, with or without operation.

Cairns [20] emphasizes the importance of heredity in polycystic disease of the kidney, and reports the occurrence of the same disease in three generations of one family.

According to Stallman,[21] cystinuria is a family and hereditary abnormality in the metabolism of protein in which cystine, a normal product of hydrolysis of proteins, is excreted in the urine in a higher content than normal. This continues throughout life. Cystine predisposes to the formation of calculi, particularly when the urine is not acid. The formation of cystine stones is dependent on the diet, and Stallman emphasizes factors in the prevention, such as the administration of large doses of sodium bicarbonate and the use of intestinal and urinary antiseptics to allay pelvic infection.

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18. Scholl, A. J., and others: A Review of Urologic Surgery, Arch. Surg. **11**:304 (Aug.) 1925.
19. Lyman, G. I.: Arch. Pediat. **42**:96-107 (Feb.) 1925.
20. Cairns, H. W. B.: Quart. J. Med. **18**:359-392.
21. Stallman, J. F. H.: Lancet **2**:375-378 (Aug. 22) 1925.

News and Comment

TEACHERS TRAINING COURSES

Courses for training teachers of sight saving classes will be given again this year at the University of Cincinnati during the summer season.

AWARD OF LESLIE DANA MEDAL

The Leslie Dana medal, given for the most outstanding achievement in the prevention of blindness and the saving of sight, will be awarded this year to Miss Louisa Lee Schuyler of New York City, who, in 1908, launched the movement for the prevention of blindness.

Abstracts from Current Literature

Anatomy and Physiology

THE TYPE OF PHAGOCYTIC CELL AND ITS RELATIVE PROPORTIONS IN HUMAN BONE MARROW AND SPLEEN, AS IDENTIFIED BY THE SUPRAVITAL TECHNIQUE, WITH SPECIAL REFERENCE TO PERNICIOUS ANEMIA. CHARLES A. DOAN, J. Exper. Med. **43**:289, 1926.

Recently, Peabody and Broun have reemphasized the presence of a relatively large number of phagocytic cells in the bone marrow in pernicious anemia. Sabin, Doan and Cunningham, by means of a supravital technic, have separated the mononuclear phagocytic cells of the spleen, bone marrow, connective tissues, and serous exudates into monocytes and clasmatocytes. The clasmatocyte, probably of endothelial origin and of recognized importance in the physiologic destruction of old red blood cells, is of particular interest in its possible relationship to another function attributed, at least tentatively, to endothelium, namely, that of being the ultimate source of the red blood cell.

The present studies were made with the purpose of determining the type of the phagocytic cell which occurs in increased numbers in the bone marrow in pernicious anemia. Preparations of living cells from spleen and bone marrow from four patients with pernicious anemia, and from six patients dying of other causes were studied by the supravital technic. Two of the patients had biopsy examinations of the bone marrow.

In the bone marrow of the patients with pernicious anemia, there was a noticeably higher percentage of clasmatocytes. In three of these cases, all fatal, the clasmatocytes showed extreme phagocytosis of red blood cells, a strikingly large number of which were nucleated. In no case did the peripheral blood show more than a very occasional normoblast.

The inference is that, in these hyperplastic marrows, abnormally stimulated clasmatocytes were not only ingesting old red blood cells but also young, immature forms which had not yet entered the general circulation. Such an interpretation indicates the large part which these phagocytic cells may play in contributing to the anomalous situation recognized in pernicious anemia, namely, that of an apparently hyperactively functioning marrow with, nevertheless, a rapidly progressive, idiopathic anemia. Fewer clasmatocytes were found in the spleen preparations of the pernicious anemia cases than in the controls.

STUDIES ON THE HISTOGENESIS OF AUTOPLASTIC THYMUS TRANSPLANTATIONS. JESSIE M. GOTTESMAN and HENRY L. JAFFE, J. Exper. Med. **43**:403, 1926.

With the hope of throwing some light on the origin of the small thymic cell, now in dispute, autoplastic transplantations of fragments of thymus were made in the abdominal muscles in albino rats, varying from 38 days to 45 days of age, and a histologic study of the transplants was made at approximately twelve hour intervals until the 106th hour, then at twenty-four hour intervals until the sixteenth day. In all, 212 transplants from fifty-three rats were studied.

The authors found that the autoplastic transplants of the thymus undergo destructive changes during the first forty-eight hours, at the end of which time regenerative changes begin. They state that these regenerative changes are characterized by proliferation of the reticular cells, which, as regeneration

progresses, leads to almost complete replacement of the transplant area by these cells so that the transplant takes on an epithelial appearance. During the third day, the small thymic cells first appear between the proliferated reticular epithelium cells, apparently as a result of enlargement and division of these latter cells. At about the sixth day, thymic lobules are formed, and during the seventh day there is beginning differentiation of these lobules into cortex and medulla. At the end of two weeks all active transplants show thymic lobules made up of cortex and medulla, which differ from the normal thymic lobules of young animals only in that they are smaller and irregular.

Emphasis is placed on the fact that the time of appearance of the small thymic cells coincides with the period of most active division of the reticular cells, and that even on the sixth day when the lobules are composed almost entirely of round cells, it is unusual to find mitotic figures in the round cells.

The authors conclude that the small thymic cells arise from the reticular epithelium in the regeneration of the transplant.

McCLURE, Evanston, Ill.

THE NORMAL WEIGHT OF THE HUMAN THYMUS. A. B. BRATTON, J. Path. & Bact. **28**:609-620, 1925.

This study is based on 337 selected healthy individuals under 16 years of age who died within twelve hours of the onset of some acute disease, were killed by accident, or who died within twenty-four hours following an accident.

Average Weight of Thymus

Age	Number of Patients	Average, Gm.
Still born and under 2 days	58	11.18
2 days to 3 months	22	19.00
3 months to 6 months	10	22.85
6 months to 1 year	13	22.08
1 year to 2 years	27	26.00
2 years to 6 years	107	25.18
6 years to 11 years	68	29.00
11 years to 16 years	32	27.24
	337	

HELMHOLZ, Rochester, Minn.

ON THE ABSORPTION OF REDUCED IRON ADMINISTERED IN LARGE DOSES BY THE GASTRIC TRACT. ITALO SACCHETTO, Arch. di pat. e clin. med. **4**:554, 1925.

In 1921, Whipple and Robscheit have stated that the body was unable to absorb inorganic iron given by mouth. The author claims to disprove this statement by experiments on dogs. Three groups of animals were used: (1) control animals, (2) animals which were given colloidal iron hydroxide intravenously, and (3) animals which were fed reduced iron in varying doses over varying periods of time. The animals were killed and the organs examined for iron by Hall's method. Intravenous injection of colloidal iron hydroxide resulted in a deposit of iron in the spleen, liver and bone-marrow. Following feeding of reduced iron, increased deposit of colloidal iron was similarly found in the spleen and bone-marrow in all cases, and also in the liver if the iron had been given repeatedly over a considerable time.

HIGGINS, Cincinnati.

Pathology, Bacteriology and Biochemistry

A Study of Bacillus Acidophilus from the Digestive Tract of Calves. Marion L. Orcutt, J. Bact. **11**:115 (Feb.) 1926.

Bacillus acidophilus types were found to be always present in the small intestine of calves. The strains corresponded in general in biologic characteristics to the *B. acidophilus* types found in man and in other animals.

A Study of Enterococci from the Digestive Tract of Calves. Marion L. Orcutt, J. Bact. **11**:129 (Feb.) 1926.

Enterococcus organisms, which could be separated into four groups according to fermentation reactions, were found to be inhabitants of the digestive tract of normal calves as well as calves suffering from diarrhea or from scours. "The enterococcus differs from *B. acidophilus* in its ability to grow in a more alkaline medium, and also in being slightly less resistant to acid. . . ."

Studies in Microbic Heredity. V. The Biogenetic Law of Haeckel and the Origin of Heterogeneity within Pure Lines of Bacteria. Ralph R. Mellon, J. Bact. **11**:203 (March) 1926.

From a study on the genetic relationships of bacteria, using a strain of diphtheroid organism, isolated from a single cell, and cultures of *B. coli*, the author has drawn the following conclusions:

"1. The biogenetic law of Haeckel is capable of application to the genetic history of bacteria.

"2. The various phases of the pleomorphic cycle represent the ontogeny of a strain; when the phases are stabilized through mutation, they collectively represent the phylogeny of this strain.

"3. The bacterial classifications that widely separate the cocci from the bacilli do not find genetic support, irrespective of the practical value of such artificial division.

"4. Group and specific agglutinogens have been demonstrated between stable races of bacilli and cocci.

"5. Complete serologic reciprocity has been shown for two races of bacilli, morphologically and culturally quite diverse.

"6. Considerable biologic diversity has been shown to exist among the various phases of the pleomorphic cycle. On this fact can be appropriately based the heterogeneity of pure line cultures."

Westlund, Chicago.

The Effect of High Protein Diets on the Kidneys of Rats. Henry Jackson, Jr., and Margaret D. Riggs, J. Biol. Chem. **67**:101, 1926.

White rats were fed a diet containing 76 per cent of protein, either as casein, or as a mixture of casein and egg albumin, for a period of from ten to twenty months. In no cases did the high protein diet produce any recognizable nephritis.

The Site of Ammonia Formation and the Prominent Rôle of Vomiting in Ammonia Elimination. Sidney Bliss, J. Biol. Chem. **67**:109, 1926.

Nash and Benedict (1921) concluded that ammonia production in the body was a specialized function of the kidney because (1) in nephrectomized dogs,

the ammonia of the blood did not increase in amount, and (2) in normal animals the renal vein contains from two to three times as much ammonia as arterial blood.

The author found increases in the ammonia of the blood not only in the renal vein, but also in the splenic and pancreaticoduodenal veins. Although there is ammonia formed by the kidney, it is also formed elsewhere. The author believes ammonia formation is a generalized tissue phenomenon.

Ammonia is excreted in vomitus by nephrectomized animals, and also by patients with uremia. This would explain the failure of the blood ammonia to rise in the nephrectomized animals of Nash and Benedict.

An increase in the ammonia content of the blood was found in nephritis.

A New Method for the Identification and Estimation of Cholesterol and Certain Other Compounds. John Vernon Steinle and Louis Kahlenberg, J. Biol. Chem. **67**:425, 1926.

Cholesterol forms a definite compound with antimony pentachloride; this product is a muddy brown precipitate, which dissolves in chloroform to yield a clear cobalt blue solution. This blue color is fairly stable, and is used as the basis of a qualitative and quantitative (colorimetric) determination of cholesterol. Details of a method of determination of cholesterol in the blood are given. Phytosterol gives a similar reaction with antimony pentachloride.

The Effect of Sleep on Urinary Chlorides and *p*H. George Eric Simpson, J. Biol. Chem. **67**:505, 1926.

After awakening in the morning, there is an increase in the alkalinity and total chlorides of the urine. On falling asleep at night, there is a decrease in alkalinity and total chlorides; when sleep occurs in the day, there is a similar change in the urine.

Higgins, Cincinnati.

The Immunity Produced by the Growth of Tetanus Bacilli in the Digestive Tract. Carl TenBroeck and Johannes H. Bauer, J. Exper. Med. **43**: 361, 1926.

Guinea-pigs, with feces negative for tetanus-like bacilli and serums free from antitoxin and agglutinins for the various types of tetanus bacilli, on three different days were fed heated washed sediment from old bouillon cultures of tetanus bacilli. One lot of these pigs was given spores from type I, another type III, and a third type V cultures. About six months later, the blood serums of these animals were found to contain agglutinins for the type of bacillus fed, but none for the other types. Antitoxin was present in all. Subsequently, spores from known types of tetanus cultures, suspended in an aleuronat preparation, were injected intramuscularly into these animals.

When injected with the culture fed, the animals failed to develop tetanus. When injected with a culture of a type other than that fed, they developed tetanus and died at the same time as the controls, in spite of the fact that their serums contained considerable antitoxin.

In a few tests, it was found that guinea-pig carriers of one culture of type V were resistant to other cultures of the same type, thus showing the immunity to be specific for the serologic type.

That the immunity due to feeding is not absolute was shown in some earlier experiments, in which spores were inserted under the skin in glass capsules

subsequently crushed. Here guinea-pigs died following inoculation with the same culture which had been fed.

Experiments were done with feeding of mixtures of types of tetanus spores, with the result that most of the animals became immune to all the types tested. All the types were agglutinated by the serums. Antitoxin was found in the serums in amounts approximately as in animals fed a single type.

Stock guinea-pigs having tetanus-like bacilli in stools and antitoxin in the blood, showed little, if any, resistance to injection of tetanus toxin.

The authors believe that antitoxin plays little part in acquired immunity to tetanus, but that there are other bodies, specific for type, which protect animals against infection.

They have seen two cases of tetanus in persons from whose stools tetanus bacilli were obtained. In one, the bacillus was the same serologic type as that causing the infection; the type of the other was not determined. Both patients recovered.

McCLURE, Evanston, Ill.

STUDIES IN MICROBIC HEREDITY. III. THE HEREDITARY ORIGIN OF GROUP AND SPECIFIC AGGLUTINOGENS AMONG THE COLON-ALKALIGENES ORGANISMS. R. R. MELLON and E. YOST, J. Immunol. **11**:139, 1926.

B. alkaligenes can grow in the human body as a large gram-positive diplococcus and propagate itself for years as such on artificial mediums. By mutation it will dissociate into a bacillary stage and into a streptothrix-like stage and into a stage of mixed morphology, all of which will breed to their own types. There is evidence that this mutation process involves a primitive sexual cycle (zygospore formation) which appears to exist for this organism and *B. coli*. The type of pleomorphism here shown is directly comparable to the pleomorphism of the fungi, and strengthens the belief that bacteria are not monomorphic but are fungi imperfecti. Serologic interrelations have been shown to exist between these stabilized stages (variants) in the life history of a single organism. Group and specific agglutinogens have been shown to exist among these stages as well as between them and *B. coli*. The demonstration of the genetic history of this organism has made possible the discovery of group agglutinins in a serum that would conventionally be regarded as having only the specific variety. The failure to recognize the group agglutinins by usual agglutination technic is referred, first, to the presence of an inhibitory factor probably common to all serums, and second, to its selective adsorption by the strain in question. An almost identical variant serologically was but slightly affected by the inhibitory substance. The results show clearly that serologic reciprocity does not of necessity imply identity in other respects.

STUDIES IN MICROBIC HEREDITY. IV. OBSERVATIONS ON GROUP AGGLUTININS IN SPECIFIC SERA WITH THE TECHNIC OF CATAPHORESIS. R. R. MELLON and E. GRENQUIST, J. Immunol. **11**:161, 1926.

The cataphoresis method as applied to certain anomalies of the agglutination reaction confirms and extends the work of R. R. Mellon which deals with the hereditary origin of group and specific agglutinogens. It indicates that group agglutinins may be present in so-called specific serums, but their presence may not always be detected by standard methods for this test. With the strains in question, the authors obtained results by employing a sensitization temperature of 20 C. instead of 37 C., which in some cases was reinforced by extending the time of observation. An explanation of the observation

may rest on the apparent fact that some strains appear to have greater avidity for a nonspecific serum inhibiting factor at 37 C. than for group agglutinin, but that at 20 C. this effect is somewhat compensated. With one of the strains studied (K 84) either the products of autolysis or an inhibitory medium substance prevented the decrease of the electrical charge that occurred after washing the strains. Strains that appear to absorb specific agglutinin strongly show a noteworthy decrease in potential in immune serum. Moreover, this lowered charge may be still further decreased by washing the excess of immune serum from the organisms. On the other hand, washing off the immune serum from a sensitized organism had an opposite effect on a feebly binding strain. This effect consisted in a return of the decreased charge to its original level, or even to higher levels than it possessed before its subjection to the action of immune serum.

S. A. LEVINSON.

RELATIONSHIP OF INCUBATION TEMPERATURE TO VIABILITY, RATE OF GROWTH AND TOXIN PRODUCTION OF CLOSTRIDIUM BOTULINUM IN DIFFERENT VEGETABLES. WILLIAM A. STARIN, J. Infect. Dis. **38**:106 (Feb.) 1926.

Temperatures of 20 and 25 C. are equally suitable for the growth of *Clostridium botulinum,* and for the production of botulinus toxin in such vegetables as corn, string beans, peas, and spinach. The rate of development is somewhat more rapid at 25 than at 20 C., although in each case the toxicity eventually reaches the same level.

A temperature of 10 to 12 C. is not suitable for growth of *Clostridium botulinum,* nor for the production of a potent toxin, even when incubation is extended to five months.

Death of the organism does not occur at any temperature used, even after three months' incubation. Even in those mediums in which no evidence of growth or toxin production could be detected, transplants to a suitable medium, such as beef heart, resulted in abundant growth of the organism with normal toxin production.

Disintegration of the medium parallels the production of toxin, although in some instances lethal doses of toxin may be present with practically no noticeable changes in the gross appearance or the odor.

The four vegetables used ranked as follows in the rate of toxin production, and in the quantity of toxin produced: corn, peas, string beans, spinach.

The high initial acidity of the beans and spinach may be responsible for the slight growth and toxin production in these mediums.

PULMONARY INFECTIONS BY FRIEDLÄNDER'S BACILLUS. WILLIAM P. BELK, J. Infect. Dis. **38**:115 (Feb.) 1926.

Eighteen cases of infection of the lung by *B. mucosus* were studied, and a provisional report is made of a chronic pulmonary lesion caused by this organism. Six cases of lobar pneumonia due to *B. mucosus* are reported in detail, with reference to thirty-eight cases in the literature.

THE GERMICIDAL PROPERTIES OF SOAP. JOHN E. WALKER, J. Infect. Dis. **38**:127 (Feb.) 1926.

The meningococcus is killed in two and one-half minutes by N/80 to N/640 solutions (from 0.4 to 0.04 per cent) of the soaps of the fatty acids ordinarily present in soap bases: 1 per cent phenol (carbolic acid) is required to kill under the same condition.

The gonococcus is killed in two and one-half minutes by N/640 to N/5,120 solutions (from 0.004 to 0.006 per cent) of the same soaps; 0.5 per cent phenol killed under the same condition.

Sodium resinate also possesses marked germicidal activity toward these two organisms.

The meningococcus, on being tested with four commercial soaps, showed approximately the same degree of susceptibility as would have been anticipated from the action of the chemically pure soaps.

The susceptibility of meningococci and gonococci is such that they (along with streptococci, pneumococci and diphtheria bacilli) will be readily killed by any ordinary soap used with a reasonable degree of care.

The dysentery bacilli and paratyphoid bacilli react to the different soaps in the same manner as previously shown for typhoid and colon bacilli, that is, they are killed by moderate concentrations of the soaps of the saturated acids, but are completely resistant to the soaps of the unsaturated acids at ordinary temperatures.

The most readily available commercial soap to be used against the typhoid bacilli, paratyphoid bacilli, and dysentery bacilli is salt soap prepared exclusively from coconut oil.

BIOLOGIC SIGNIFICANCE OF THE SOLUBLE SPECIFIC SUBSTANCES OF PNEUMOCOCCI. LLOYD D. FELTON and G. HOWARD BAILEY, J. Infect. Dis. **38**:131 (Feb.) 1926.

The soluble specific substance of type 2 pneumococcus, prepared according to a method which eliminates all except a minimum amount of nitrogen, was injected into mice in extremely small doses, together with attenuated type 2 pneumococci. The results indicate an antagonistic effect on the defense of the animals, or an actual increase in the virulence of the mirco-organisms from ten to one hundred fold. The injection of the specific substance alone into mice in doses many times greater than used with the attenuated cultures of pneumococci demonstrated that the lots of specific substance used were in themselves nontoxic.

Experiments are recorded which show that the protective substance of antipneumococcus serum and antibody solutions are neutralized both in vitro and in vivo, and indicate that the neutralization is approximately in proportion to the amount of soluble specific substance present. Furthermore, the results indicate that the soluble specific substance must be considered at least as one probable source of the antagonistic effect commonly noted in protection tests with the larger amounts of antipneumococcus serums and antibody solutions. These serums and solutions, when treated even with very low concentrations of the specific substance, exhibit to a marked degree the common zonal phenomenon in regard to protection, which appears to be entirely analogous to that obtained in certain instances with untreated antipneumococcus serums and antibody solutions. This analogy appears to have a certain degree of confirmation in the experiments recorded, in which it was shown that precipitable "residues" may be extracted from such serums and solutions.

It would appear that the soluble specific substance of type 2 pneumococcus used in the present investigation, assuming that the results are due to an actual increase in the virulence of the attenuated culture of this organism, produced an effect more or less similar to that reported by Rosenow in case of the so-called "virulin". A great deal more experimental work must be carried out, using a soluble specific substance of unquestionable purity, before it might be possible to suggest an identity or even a relationship between the latter substance and the hypothetical one just mentioned.

THE SPECIFIC PRECIPITATES OBTAINED FROM ANTIPNEUMOCOCCUS SERUM AND ANTIBODY SOLUTION BY THE SOLUBLE SPECIFIC SUBSTANCES OF PNEUMOCOCCI. LLOYD D. FELTON and G. HOWARD BAILEY, J. Infect. Dis. **38**:145 (Feb.) 1926.

With appropriate amounts of the soluble specific substance, all the protective substance in type 2 pneumococcus serums may be precipitated. The precipitate so obtained is practically insoluble in water, sparingly soluble in 3 per cent sodium chloride, and very soluble in dilute acid and alkali when the salt content is low. The hydrogen ion concentration of minimum solubility of one sample tested is *p*H 6.6.

Further chemical and biologic characteristics of the precipitate are pointed out.

BEHAVIOR OF BOTULINUM TOXIN IN ALIMENTARY TRACT OF RATS AND GUINEA-PIGS. GAIL M. DACK, J. Infect. Dis. **38**:174 (Feb.) 1926.

Botulinum toxin when mixed with stomach tissue and abdominal wall tissue from guinea-pigs and mice in vitro, and incubated at 35 C. for one hour was not reduced in potency, except in two cases in which the stomachs of mice were used. The reduction, however, was slight in these cases.

Botulinum toxin was not completely destroyed in the stomachs and small intestines of rats and guinea-pigs receiving injections of the toxin directly into the stomach. Its presence was definitely demonstrated after twelve hours in guinea-pigs and after three hours in rats.

In two cases out of seven, toxin was demonstrated in the blood of guinea-pigs fed with botulinum toxin. No toxin was found in the blood of rats fed with large doses of botulinum toxin. Toxin was found in the blood of rats and guinea-pigs three hours after intravenous and intramesenteric injections of the toxin.

KENNEDY, Rochester, Minn.

IMMUNOLOGICAL NOTES. VII-XVI. A. T. GLENNY, C. G. POPE, HILDA WADDINGTON and U. WALLACE, J. Path. & Bact. **28**:463-482, 1925.

Horses are given a primary immunizing injection of toxin-antitoxin mixture, and then an interval of one month is allowed to elapse before any more tetanus toxin is injected. Such horses produce a much higher grade of antitoxin than those not allowed to rest. The average value of the serum from ten horses having no rest was 155 antitoxic units; that of six horses having one month's rest, 450 antitoxic units.

HELMHOLZ, Rochester, Minn.

CONGEALING OF TISSUES: A PROCEDURE TO OBTAIN AUTONEUROTOXIN AND OTHER CELLULAR AUTOTOXINS. A. SPERANSKY, Ann. de l'Inst. Pasteur **60**:213 (March) 1926.

The author has found that by means of freezing with compressed gases, sharply limited areas of the cortex may be congealed through a trephine opening, without disturbing the brain membranes. After the effect of the anesthetic has passed off, the animals so treated seem normal for a time, but after a few hours develop signs of a diffuse toxic encephalitis, with signs closely resembling epilepsy. The extent and duration of these attacks is proportional to the period of freezing, and usually results in death within a few hours. These signs do not seem to be due to focal irritation, since the manifestations are similar regardless of the location of the lesion produced. If

the congealed area is removed immediately after it is produced, the animal makes an uneventful recovery; if removed after a lapse of one or two hours, the outcome is not modified. By submitting an animal to several sublethal "doses" of congelation, a degree of immunity is produced. There is some evidence that the eschar from one animal when introduced beneath the dura of another sound animal may produce similar immunity.

The condition is ascribed to the development of an autotoxin. Analogous treatment of other tissues of the body has offered similar results. The autotoxin seems specific for the same type of tissue. By congealing part of one kidney, lesions were produced in the other. The author proposes that the principle may be applied in the treatment of new growths. By congealing a part of the growth, the elaboration of the specific autotoxin may lower the resistance of the neoplasm to such an extent that it will lose its invasive powers, and may be combated by the normal body tissues.

BOYD, Iowa City.

RIB IMPRESSIONS ON THE LUNGS OF INFANTS. T. KONSCHEGG, Virchows Arch. f. path. Anat. **259**:225, 1925.

Furrows made by the ribs on the surface of the paravertebral portions of the lungs of infants are frequently seen. They may number one to ten. Factors in their formation are emaciation and increased intra-abdominal tension, the latter leading to decreased diaphragmatic breathing with greater distention of the upper portions of the lungs through the action of the accessory muscles of respiration.

O. T. SCHULTZ.

I. THE STUDIES ON THE MENINGOCOCCI VARIABILITY OF MENINGOCOCCI. II. CLASSIFICATION OF MENINGOCOCCI ON BASIS OF AGGLUTININS. III. RELATIONSHIP BETWEEN AGGLUTININ REACTION AND SUGAR FERMENTATION. S. KONDO, Tohoku J. Exper. Med. **6**:399, 1925.

The changes in the agglutinability of meningococci depend on the development of variants that resist agglutination. In order to maintain a strain of constant agglutinability, it is necessary to transplant from a colony that is found to be agglutinated in typical fashion by the homologous serum.

By the use of serum produced with pure strains as described, Kondo found that forty-three meningococcus strains could be divided into thirteen types, which does not represent, however, all the types of meningococcus in nature.

Kondo found that while meningococci may be divided into groups according to their power to ferment levulose, maltose and dextrose, yet these groups do not correspond with serologic groups.

[ARCH. PATH.]

Nutrition

A STUDY OF RICKETS. DONALD PATTERSON and RUTH DARBY, Arch. Dis. Child. **1**:36 (Feb.) 1926.

In 339 London infants examined clinically and by roentgenogram, only four cases of active rickets were found. One hundred and ten cases showed healed rickets. A vague history of the previous administration of cod liver oil was given in 92 per cent of the cases. The authors concluded that the oil was effective both prophylactically and therapeutically.

PETERMAN, Milwaukee.

NUTRITIONAL KERATOMALACIA. A. B. SCHWARTZ, J. A. M. A. **85**:2025 (Dec. 26) 1925.

The author reports a case of keratomalacia in an infant following a diet restricted for therapeutic purposes. This constitutes an almost experimental production of the disease. Besides the usual weight loss and nutrional upset, the infant presented pronounced meningeal symptoms. Recovery followed administration of cod liver oil and a diet of whole lactic acid milk.

BONAR, Salt Lake City.

THE ANTIRACHITIC VALUE OF IRRADIATED CHOLESTEROL AND PHYTOSTEROL. V. CHEMICAL AND BIOLOGICAL CHANGES. ALFRED F. HESS, MILDRED WEINSTOCK and ELIZABETH SHERMAN, J. Biol. Chem. **67**:413, 1926.

Anhydrous pure cholesterol is rendered antirachitic by ultraviolet irradiation; thus it is the sterol and not an impurity which was the active product in previous work.

As cholesterol acetate, an ester of the unsaturated cholesterol, is rendered antirachitic on irradiation, and dihydrocholesterol, a saturated reduction product, is not, it would appear that the double bond in the cholesterol molecule is an essential factor in its activation.

Comparing irradiated and nonirradiated cholesterol, the former had a greater inhibiting action on hemolysis caused by digitonin, and also was not so completely precipitated by digitonin.

THE IRON CONTENT OF MEATS. E. B. FORBES and RAYMOND W. SWIFT, J. Biol. Chem. **67**:517, 1926.

The authors have analyzed many samples of meat for their iron content. To avoid the common error of contamination of the samples, a bronze knife and a bronze meat chopper were used.

The following gives some of the results found:

	Iron Per cent	Protein Per cent	Fat Per cent
Bacon, cured	.0013	10.4	64.1
Ham, cured	.0014	21.1	13.6
Pork	.0015	19.0	12.5
Lamb	.0016	19.6	6.1
Beef	.0025	20.7	5.8
Veal	.0025	21.9	1.6
Beef heart	.0044	16.2	4.9
Beef brain	.0053	10.5	7.9
Beef liver	.0082	20.6	4.7
Beef spleen	.0138	18.9	1.9
Beef kidney	.0188	16.1	1.9
Beef blood	.0444	17.9	...

Beef and veal contain 66 per cent more iron than pork or lamb, twice as much iron as potatoes and ten times as much as milk.

The organ meats, especially the liver, spleen and kidney contain much more iron than the muscles.

There is more iron in peas, beans, graham flour, oatmeal and spinach than there is in beef.

HIGGINS, Cincinnati.

IRRADIATION OF FOODSTUFFS WITH ULTRAVIOLET LIGHT. HELEN M. M. MACKAY and HAROLD F. SHAW, Lancet **1**:8 (Jan. 2) 1926.

Observations of the effect on rachitic children of foodstuffs irradiated for one hour at one foot distance from a mercury arc were carried out; twenty-

four hours supply was irradiated daily. Weekly roentgenograms were taken of the long bones of the children.

Three children received irradiated dried milk, one irradiated sweetened condensed milk, and two irradiated dried milk which had been boiled ten minutes after irradiation. All showed calcification of the bones at a rate equal to that usually obtained by direct irradiation or by administration of cod liver oil.

Two children were given 3 ounces of irradiated white flour. One gave a negative result; the other result was inconclusive, probably negative.

One child was given 6 drachms (25 cc.) of irradiated cottonseed oil; there was very slow healing of the bone lesions. One child suffering from infantile tetany was cured by irradiated dried milk.

LANGMANN, New York.

IMMUNIZATION PROPERTIES IN AVITAMINOSIS AND IN STARVATION. G. PARRINO and P. LEPANTO, Bol. d. Ist. sieroterapico Milanese **4**:319, 1925.

Starvation and avitaminosis lead in guinea-pigs and pigeons to loss of weight, lowering of the temperature and reduction of the normal and artificially evoked immune properties. In addition, in starving guinea-pigs there is an increase in the neutrophil polymorphonuclear leukocytes, while in avitaminosis there is lymphocytosis. In guinea-pigs both conditions are accompanied by a pseudo-esosinophilia. Avitaminosis causes more marked changes than starvation.

SECRETORY ACTIVITY OF THE NONGRAVID MAMMARY GLAND. L. LITTEN, Virchows Arch. f. path. Anat. **259**:126, 1926.

Litten made a histologic study of mammary glands of eighteen nonpregnant women in whom a milky secretion could be expressed from the nipple. In four of these the condition was due to simple retention after normal lactation. In five cases the phenomenon occurred during the menstrual or premenstrual stage and was associated with the acinar hyperplasia of the mammary gland which Rosenberg had described as a normal phenomenon of the menstrual cycle. In the remaining nine cases secretory activity bore no relation to the menstrual cycle and was noted especially in older women, some of whom had passed the menopause and whose breasts contained cysts or adenomas. For the last named group Litten proposes the term pathologic lactation, as contrasted with the postpartum retention lactation and menstrual lactation of the other two groups.

O. T. SCHULTZ.

THE ACTIVITY OF STOMACH LIPASE IN NATURAL AND FOREIGN WHEY. M. LANDSBERGER, Ztschr. f. Kinderh. **39**:665, 1925.

In agreement with Davidsohn, it is found, using the stalagmometric method, that the cleavage of tributyrin occurs by the action of lipase obtained from the stomachs of infants, more quickly in human milk whey than in cows' milk whey. The cause of this phenomenon does not lie in the difference in the degree of

ionization of the salts but in the colloidal substances, because the action of the lipase goes on with the same rapidity in both kinds of whey when they are freed from albumin.

THE HORMONE THERAPY IN RICKETS. L. LANGSTEIN and H. VOLLMER, Ztschr. f. Kinderh. **39**:751, 1925.

Fresh preparations of hypophysis, thymus, ovary and thyroid with hydrous wool fat are rubbed in on the skin on the assumption that rickets may be due to an endocrine disturbance. Three children recovered under this treatment, but one recovered by simple massage with petrolatum.

EMERSON, Boston.

Prenatal Conditions

CONGENITAL STENOSIS OF THE ESOPHAGUS. JOHN H. FITZGIBBON, Northwest Med. **25**:94 (Feb.) 1926.

Fitzgibbon reports the condition discovered soon after birth. Gastrostomy was performed first, and the existence of communication between the mouth and stomach was established by the passing of a silken thread by means of a cystoscope and urethral catheter. By this thread, piano wire was passed through the opening, and dilatation secured by the passing of olive bulbs. This was quite successful but the patient succumbed to an intercurrent infection.

Another patient, aged 14, had difficulty in swallowing from birth, being able to take only liquid and soft food. This boy at the age of 7 had had a gastrostomy (now closed), and subsequent dilatation. At the time he was first seen, swallowing had become almost impossible. A small wire guide was passed through the stricture which was 10.5 inches from the incisor teeth. Over this wire, bougies were passed. The stricture had been enlarged to No. 24 French, and all kinds of food could be swallowed. The stricture was due to a congenital web, as it was very short, and offered slight resistance to the bulbs.

SCOTT, Philadelphia.

CHONDRODYSPLASIA. WALLACE COLE, Surg., Gynec. & Obst. **43**:359 (March) 1926.

According to Ollier, this disease is an affection of the period of body growth, characterized by an arrest of the growing parts of the skeleton, nodosities and swellings of the involved long bones, curving of the diaphyses, and slight but constant deformities of the hands. Molin, who has studied several cases of so-called "dyschondroplasea" describes it as an osseous dystrophy producing partial arrest of skeletal development, affecting principally the long bones of the extremities and the bones of the hands. The curvatures are analogous to those of rickets. Not infrequently, the condition involves only one-half of the body, and while the etiology is not understood, it seems certain that heredity is a strong factor. Bentzen, as a result of experimental work on rabbits, in which either the sympathetic trunk was divided or the nutrient artery to the bone was injected with alcohol, concludes that the disease may be interpreted as a typical reaction of bone to an active hyperemia due to disorders in blood vessel innervation. The author believes that it is rather difficult to classify the cartilaginous dystrophies, because there are any number of variations, ranging from those with frank multiple exostoses to those with only slight changes in the internal achitecture of the bone. The term "chondrodysplasia" should be a gen-

eral one, including all of the forms, but the term "Ollier's disease" should be limited to those which show an asymmetric involvement of the body as an outstanding feature.

MILLER, Chicago.

PROPHYLACTIC IMMUNIZATION AGAINST PUERPERAL STREPTOCOCCUS BLOOD-INFECTION. N. C. LOUROS, Monatschr. f. Geburtsh. u. Gynäk. **71**:142 (Nov.) 1925.

Six hundred and eighty-two parturient women were treated with anti-streptococcus serum, 483 at delivery and 199 before. One hundred and eighty-two patients developed complications and fever but none died. The immunized blood was able to resist the infection, even in three subjects who developed positive blood cultures of virulent streptococci.

PHYSICAL DIFFERENCES IN TWINS AND THEIR CAUSES. THEO BRANDESS, Monatschr. f. Geburtsh. u. Gynäk. **71**:249 (Dec.) 1926.

One hundred and seventy-six pairs of twins were studied; of these it was possible to establish the approximate date of impregnation in 129. Ninety-seven of the 129 were double ovum twins and thirty-two single ovum. The body weights, body lengths, and the measurements of the umbilical cords were compared. The differences in size were entirely accidental and no definite cause could be found.

PETERMAN, Milwaukee.

Diseases of the New-Born

PROPHYLACTIC TREATMENT OF THE NEW-BORN AGAINST TUBERCULOSIS BY MEANS OF THE VACCINE BCG. (1921 to 1926.) A. CALMETTE, C. GUERIN, L. NEGRE and A. BOUQUET, Ann. de l'Inst. Pasteur **60**:89 (Feb.) 1926.

After discussing various types of bacilli related to Koch's bacillus, and their transmutation, the authors describe the cultural development of the *Bacillus Calmette-Guerin* (BCG) and the vaccine developed from it. This strain of organism was obtained by growing bovine tubercle bacilli on pure beef bile medium, carrying it through 230 transplants at five day intervals. The resultant organisms had lost all their tubercle-producing powers and their virulence for domestic animals. The loss was evidently permanent, because repeated transfers through laboratory animals did not restore their lost properties.

By introducing this living organism into animals, it was possible to immunize them against tuberculous infection. This effect was associated with the persistence in the animal of the living organisms used for immunization. This type of immunity, which is found in tuberculosis, syphilis, certain protozoan infections, and probably leprosy, has been termed "premunity." The authors have premunized animals against tuberculosis by administering an emulsion of their organism by intravenous, subcutaneous or enteric routes. When given by mouth during the first few days of life, its effects are readily produced. It has been used in animals in various countries for the past eighteen months, and has seemed effective, with no unpleasant sequelae. The development and existence of premunity is not associated with any constant or typical reaction to tuberculin.

Attention is called to statistics on infant mortality due to tuberculosis. Correlating adult tuberculosis with the acquisition of infection during infancy, they

quote Behring's statement, that manifestations of tuberculosis in the adult are practically always "the last verse of a ballad sung by the mother to her nursling over its cradle." The greatest number of infections occur during the first year. In Paris, 27.8 per cent of all deaths in infants under 1 year old were due to tuberculosis.

A large number of infants from homes in which marked exposure to tuberculosis was unavoidable were premunized. When possible, this was done during the first week of life, the emulsion being given orally. A survey of the outcome in these cases shows that practically all were still alive and in apparent health many months after premunition, and living in the presence of tuberculous contamination. As a result of these observations, they conclude that "premunition of the new-born by means of BCG safeguards at least 93 per cent of infants, who without its protection would succumb to tuberculosis during the first year of life." They emphasize that tuberculin reactions are no criterion as to this form of protection.

In cases which fail to receive protection from BCG administered during the first few days of life, they postulate the existence of antenatal infection, due to the passage through the placenta of the filterable virulent elements which they have demonstrated and reported in previous studies.

Protection persists as long as the living organisms persist in the body. The effect may be prolonged by reinoculation at suitable intervals. In France alone, over 5,000 infants have been successfully vaccinated by this method. While in the nonprotected the mortality among infants from tuberculous environments is about 25 per cent during the first year, in their series of protected cases it has been less than 2 per cent. The procedure has been free from any accidents, febrile reactions or physiologic disturbance of any type.

They recommend vaccination during the first six days of life in the case of infants who must be exposed to direct tuberculous infection during the first three years of life.

BOYD, Iowa City.

FAT IN THE CENTRAL NERVOUS SYSTEM OF THE NEW-BORN. P. SCHWARTZ, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:713, 1926.

The author discusses the conception that lipoid material in the glia cells of infants is concerned with the physiologic development of myelin. He concludes that all the brains of dead new-born are pathologic. There are small hemorrhages, glia proliferations or axis cylinder changes which may be due to intra-uterine infections, asphyxia or trauma at birth. The lipoids in the glia are definitely related to the pathologic process and are not concerned with the building up of the myelin.

ROY GRINKER.

Acute Infections

THERAPEUTIC RESULTS WITH CONCENTRATED SCARLET FEVER ANTITOXIN. GEORGE F. DICK and GLADYS H. DICK, J. A. M. A. **85**:1693 (Nov. 28) 1925.

These authors have shown that the scarlet fever antitoxin may be refined and concentrated. In this way, the disadvantages of the antistreptococcus serums have been overcome. The minimum potency requirement is now such that one therapeutic dose shall not exceed 20 cc. in volume. The prophylactic dose should be one-half the therapeutic dose. The antitoxin in all cases has been injected into the muscles in the anterior aspect of the thigh. If enough antitoxin has been given, the rash will be definitely faded within twenty-four

hours, and there will be marked improvement in the general condition of the patient, especially in the most toxic cases. Comparison of results in an adequately controlled series of 100 cases of scarlet fever left no doubt that the antitoxin shortened the course of the disease, and reduced the number and severity of complications and sequelae. On account of the possibility that large amounts of toxin may be absorbed from infected sinuses, these investigators are giving two therapeutic doses of antitoxin to those with marked toxemia or septic complications associated with sinusitis. With one exception, all deaths in the antitoxin series occurred in persons who had been ill from six to ten days before the antitoxin was employed. They emphasize the necessity of giving the antitoxin early in the disease before complications have occurred and before too much damage has been done to the tissues. If administered early in the disease, and in adequate dosage, the antitoxin shortens the course of scarlet fever and reduces the number of complications and sequelae.

THE USE OF ETHER IN PERTUSSIS BY INTRAMUSCULAR AND RECTAL INJECTIONS. ALTON GOLDBLOOM, J. A. M. A. **85**:1791 (Dec. 5) 1925.

Intramuscular injections of ether were given in eighteen cases of whooping cough. What might be called a cure resulted in three cases, and definite improvement occurred in ten. One local reaction, but no necrosis, occurred in the children treated. Twenty-one children with whooping cough were given rectal injections of ether in oil. Thirteen of the twenty-one cases showed marked improvement, slight but definite improvement was seen in six cases, and no improvement in two. The author concludes that ether treatment is of value, and "that by the rectal method of administration it has been truly robbed of its sting."

BONAR, Salt Lake City.

TREATMENT OF PNEUMONIA. E. C. THRASH, J. M. A. Georgia **15**:86, 1926.

In discussing the treatment of pneumonia, the author states that children tolerate mercurochrome-220 soluble much better than adults, and it produces better results in them. Its early administration is almost a specific in the cure of pneumonia. Gentian violet is milder in action, and should be used instead of mercurochrome when the heart or kidneys are seriously affected, or when the shock of reaction might not, for any other reason, be safe.

MASHBURN, Atlanta, Ga.

ANATOMIC OBSERVATIONS ON THE YELLOW FEVER PROBLEM IN AFRICA. W. H. HOFFMAN, J. Trop. Med. **29**:69 (March 1) 1926.

Hoffman examined four kidneys from patients dying from a disease simulating yellow fever, occurring in the Gold Coast Colony in Africa. He quoted his previous experience of finding casts of lime salts in the kidneys of twenty-four out of twenty-eight patients dying of yellow fever in San Salvador. He found that the severe nephritic degeneration, the hemorrhages and the blood casts characteristic of the yellow fever kidney were not present, and that the necrotic desquamation of the epithelium and the lime casts, found only in this disease, were also absent. He concludes, therefore, that the disease was not yellow fever, and that it is often impossible to differentiate certain cases of hemoglobinuric fever from yellow fever, without cultural and immunologic studies.

SCOTT, Philadelphia.

ANOXEMIA IN LOBAR PNEUMONIA. CHRISTEN LUNDSGAARD, Medicine **4**:345, 1925.

In from 10 to 20 per cent of patients with lobar pneumonia, disturbances in the respiratory functions of the lungs cause an abnormally low oxygen saturation of the arterial blood. This in turn gives rise to a decrease in the amount and tension of the oxygen of the capillary blood.

Through physiologic and pathologic investigations it is demonstrated that when a decrease in the arterial oxygen content (and consequently also in the oxygen content and tension of the capillary blood) exceeds a threshold of 15 to 20 per cent, a group of pathologic symptoms appears in normal individuals. The main symptoms are: Cyanosis, mental disturbances, abnormal irritation of the nervous centers in the medulla, particularly of the respiratory center, probably an impairment of the function of the muscular system, particularly of the myocardium.

The term anoxemia is in most instances used to indicate the condition characterized by these symptoms. In other instances anoxemia simply means the underlying pathologic condition, namely, the incomplete oxygen content of the blood.

An attempt has been made to show by analyses of different facts published in the literature that the various anoxemic symptoms in the main appear at the same threshold level of arterial oxygen unsaturation. The presence or absence of a cyanosis may therefore in most instances serve as a clinically useful criterion for the presence or absence of an arterial oxygen deficit extensive enough to give rise to other less characteristic anoxemic symptoms.

In pneumonia similar symptoms are frequent. A deeper analysis of these symptoms shows first, that anoxemia probably plays a part in their development, secondly, that anoxemia is to be looked on only as one of the causes of these symptoms. To what extent some of the most important functional disturbances in pneumonia, namely, dyspnea and heart failure, are caused by anoxemia and to what extent by other factors, is not known.

In a considerable number of pneumonic patients with abnormally low arterial oxygen saturation, treatment with oxygen inhalation has caused the abnormal oxygen unsaturation to disappear. At the same time the anoxemic symptoms, especially the cyanosis, have either disappeared or decreased in intensity.

AUTHOR'S SUMMARY.

SUDDEN DEATH FOLLOWING PROPHYLACTIC INOCULATIONS AGAINST DIPHTHERIA. JESSE R. GERSTLEY, M. Clin. N. Amer. **9**:1417 (March) 1926.

Two days after the administration of the third dose of T and A mixture, a girl, aged 7 years, developed a rash on the face, vomited and became very tired and weak. The vomiting continued for two days, and was followed by stupor and coma on the fifth day. On admission her temperature was 103 F., and she was irrational. There was an erythematous rash on the face, internal strabismus and the pupils were dilated and immobile. The neck was rigid and the Kernig and Brudzinski signs were present. Leukocytes numbered 26,000; red cells, 2,000,000. The spinal fluid was found to be normal on several occasions. The urine contained albumin and a large amount of blood. Two days later a blood transfusion of 200 cc. was made, and signs of a hemiplegia, paralysis of the muscles of the left side of the face and twitchings of the muscles of the right arm and leg developed a few hours later. Death soon followed. Necropsy disclosed a blood clot covering much of the left hemisphere, acute hemorrhagic

glomerular nephritis, acute interstitial myocarditis and ecchymoses beneath the skin and dura.

While no definite conclusion has been reached as to the cause of the condition, the following possibilities are considered:

That diphtheria toxin alone was used instead of the T and A mixture, since it was afterward learned that the injection was given not by a physician but by a pharmacist who worked in a laboratory.

That a mixture was used in which the antitoxin had by some means become inactive.

That the child had a preexisting nephritis.

That the cerebral hemorrhage following transfusion may have come from blood vessels previously damaged.

SMITH, Ogden, Utah.

CASE OF KALA-AZAR? F. I. POYNTON, Proc. Roy. Soc. Med. (Section for the Study of Disease in Children) **19**:5 (Nov.) 1925.

The patient, a girl, aged 5 years, was in Malta for sixteen months. At the age of 20 months and while there, she had one attack of colitis. One year after her return to England, she suffered from vomiting and was slightly jaundiced. Six months later, Oct. 19, 1920, she lost her appetite, became sleepy, feverish, tired, and her color became sallow. She improved at first somewhat, but since February of this year she has grown worse. The abdomen has been growing larger since December, 1924. On admission to hospital, the abdomen was 22½ inches in size; the liver and the spleen were enlarged; the red blood cells were 3,760,000; white cells 1,560, of which 1,200 were lymphocytes; the Wassermann reaction was negative. The Van den Bergh test showed a slightly increased bilirubin in the blood (1 unit), the direct reaction being negative. There were no bile pigments in the urine. The formol-gel test was strongly positive. Sir Leonard Rogers examined the patient, and considered that the condition was probably kala-azar. Cultures for the organism were being made. Liver puncture would probably be necessary.

WILLIAMSON, New Orleans.

DYSENTERY ANATOXIN. J. DUMAS, RAMON and SAID BILAL, Ann. de l'Inst. Pasteur **60**:134 (Feb.) 1926.

Diphtheria toxin, when treated by heat and addition of formaldehyde, becomes inoffensive, but has antigenic properties capable of conferring immunity. The product so obtained is termed diphtheria anatoxin. In this article, the authors describe a dysentery anatoxin prepared in a similar manner, and describe its efficacy. Its ultimate value has not been determined, but results have been encouraging.

BOYD, Iowa City.

PARATYPHOID FEVER IN EARLY CHILDHOOD. WALDEMAR SCHMIDT, Ztschr. f. Kinderh. **39**:681, 1925.

In thirteen cases of paratyphoid fever B reported, the course was very mild and in some instances the diagnosis could not have been made were it not for the presence of an epidemic. It may be that the source of this infection was from cultures which were being used at the time to stamp out a plague of mice. Such cultures should not be used, particularly in institutions.

EMERSON, Boston.

Chronic Infections

THE TREATMENT OF TUBERCULOUS PERITONITIS BY OXYGEN INFLATIONS. E. W. HAYES, Am. Rev. Tuberc. **13**:27 (Jan.) 1926.

Oxygen gas in amounts varying from 200 to 1,200 cc. is introduced into the peritoneal cavity by means of a pneumothorax apparatus. It seems to be the simplest and most efficient form of treatment, and is applicable to both the exudative and nonexudative types of tuberculous peritonitis. Even in advanced and complicated cases, its palliative effect warrants a trial. In the ulcerative type of tuberculous enteritis, it is the best means we have of relieving symptoms, and in early cases may bring about a cure. Its value has also been demonstrated in the treatment of the more acute forms of tuberculous abscess, in the absence of sinuses or mixed infection.

SMITH, Ogden, Utah.

VALUE OF NONSPECIFIC PROTEIN THERAPY IN SYPHILIS. SIGMUND S. GREENBAUM and CARROLL S. WRIGHT, Arch. Dermat. & Syph. **12**:858 (Dec.) 1925.

"Nonspecific protein therapy alone will result in partial or complete involution of secondary and tertiary lesions. When used as an adjunct to neo-arsphenamine in the treatment of patients with latent syphilis with a strongly positive Wassermann reaction, the influence in reducing a positive reaction to negative is more marked than when neo-arsphenamine is used alone.

"It is suggested that the protein therapy serves to stimulate normal protective mechanisms within the body."

"Nonspecific protein therapy should prove a valuable adjunct to the usual antisyphilitic remedies."

JEANS, Iowa City.

THE DIAGNOSIS OF CLINICAL HILUM TUBERCULOSIS. JOHN B. HAWES, II, Boston M. & S. J. **194**:91 (Jan. 21) 1926.

In reading this article, one might think the author a pessimistic physical diagnostic nihilist, did not one's own findings coincide with the author's experience and conclusions, namely, for a positive diagnosis:

1. Definite exposure.
2. Real malnutrition and real underweight.
3. Ease of tire. Being tired all the time.
4. Temperamental changes. (Unrelieved by castor oil.)

Then also of importance but not essential to a diagnosis:

5. A positive Pirquet reaction.
6. Roentgen-ray evidence of marked hilum changes.

For a Negative Diagnosis.—1. Presence of tonsils, adenoids, etc., that can account for symptoms.

2. Apparent but not real underweight.
3. Negative Pirquet reaction, repeated in absence of factors that would tend to make it negative.
4. Absence of ease of tire and fatigue.

Then also of value but not essential in making a diagnosis:

5. Negative roentgen-ray evidence.

GENGENBACH, Denver.

FAMILY HISTORY IN RELATION TO PROGNOSIS OF PULMONARY TUBERCULOSIS. A. P. FORD, Tubercle **7**:117 (Dec.) 1925.

A careful inquiry into the family histories of over 1,000 patients with pulmonary tuberculosis, including only those in whom tubercle bacilli had been demonstrated in the sputum, showed a parental incidence of the disease of only about 20 per cent. Patients with a maternal history of tuberculosis were fewer than those with a paternal or no history, and acute cases were also less frequently encountered in this group.

These findings suggest that tuberculous mothers confer on their children some degree of immunity, either active or passive, which renders them less susceptible to the disease, and which offers them a better chance of recovery should they acquire it.

THE RESULTS OF THE INTRACUTANEOUS TUBERCULIN TEST IN AN ONTARIO SURVEY OF SCHOOL AND PRESCHOOL CHILDREN. J. H. ELLIOTT, Tubercle. **7**:122 (Dec.) 1925.

As a part of a general health survey of 1,392 children of school and preschool age, living in a typical Ontario town and adjoining rural township intracutaneous tuberculin tests and single roentgen-ray films of the chest were made. Thirty-two per cent reacted to the tuberculin, of whom about 10 per cent were considered to have active tuberculosis. The incidence of positive reactions at different ages were: 15 per cent at time of entering school; 25 per cent at 7 years; 40 per cent at 10 years, and 50 per cent at 15 years.

A study of the roentgen-ray films leads to the conclusion that a diagnosis of either lymphatic or early pulmonary tuberculosis was not warranted by this means alone. Increased density of the hilum and larger trunk shadows were found in a large percentage of children giving a history of respiratory infections, but without other evidence of tuberculosis.

SMITH, Ogden, Utah.

BACTERIOLOGIC FINDINGS IN CHILDREN OF LEPERS: NASAL LESIONS. F. SOLIS and H. W. WADE, J. Philippine Islands M. A. **5**:365, 1925.

Of 250 children of lepers, 35 had lepra bacilli in the nose, but in not a single instance were nasal smears positive in the absence of skin lesions. The results indicate that nasal lesions are secondary manifestations in young children, and that the nasal mucosa is not frequently the site of the initial lesion in leprosy. Indeed, they suggest that, at least in young children, the initial lesion does not occur here at all, although there is reason to believe that occasionally such may be the case in older persons.

[ARCH. PATH.]

THE POLYDACTYLITIS OF HEREDITARY SYPHILIS IN NURSLINGS. LEREBOULLET, SAINT GIRONS and GOURNAY, Arch. d. méd. d. enf. **28**:665 (Nov.) 1925.

This monograph on syphilitic dactylitis in infants was presented at the regular meeting of the Paris Pediatric Society in April, 1925. The writers review the literature of the affection since a name was first given to the symptom by Chassaignac in 1859, giving credit, moreover, to Plenck of Vienna, who, in 1779, first described the characteristic lesions.

They express some surprise at the infrequent allusion to this condition in the current medical press, fairly common though it appears to be in all countries

and readily amenable to treatment. A case is reported in an infant, aged 2½ months, with involvement of eight fingers, in addition to both radii, the ulnar bones and the tibiae. Radiologic studies are illustrated fully and the satisfactory treatment by mercurial inunctions is strongly endorsed.

DIFFICULTY OF DIAGNOSIS IN TUBERCULOSIS OF INFANTS. VLADIMIR MIKULOWSKI, Arch. d. méd. d. enf. **28**:675 (Nov.) 1925.

Mikulowski points out how important a rôle infantile tuberculosis plays in the general morbidity and mortality, not only of Poland, but of all Europe. According to Kopec, 12.8 per cent of the sick children at the Charles and Mary Hospital at Varsovia had tuberculosis in the acute stages. He notes the ease with which the meninges are involved in early infancy, and the extreme difficulty of differential diagnosis unless early lumbar puncture is resorted to.

The various clinical signs are discussed, the author asserting that his experience warrants the conclusion that the so-called Brudzinski sign is the most constant and the most easy to provoke. He has found the Kernig sign frequently absent and the Babinski sign commonly present in children under 2 years.

The "cheek sign" and the "pubic sign" of Brudzinski are also considered as valuable collateral evidence. The refractometric index of the cerebrospinal fluid described first by Jouscher, furnishes additional information for the clinician and enables him to differentiate inflammatory states in the meninges from meningeal irritation.

Mikulowski calls attention to the extra difficulties of diagnosis presenting among Polish physicians by reason of the widespread epidemics of typhoid fever now prevailing in Eastern Europe and the common invasion even in infancy. The author believes, contrary to opinion in England and America, that patients with tuberculous meningitis may go on to complete recovery.

Another form of acute tuberculosis, that of the tracheobronchial glands, is given extended consideration, and the new sign evolved by Genevrier — transmission of the cardiac sounds under the clavicle and into the right axilla — is mentioned as helpful. When pulmonary tuberculosis is suspected, examination of the stools is urged, the author invariably finding the bacillus of Koch in active cases, following the work of Venot and Moreau. He recommends that complement deviation, as practiced by Bordet and Gengou, be ascertained in each case and mentions the value of determining the colloidal resistance of the blood plasma.

AMESSE, Denver.

TUBERCULOSIS AT VARIOUS AGES; ANATOMIC EXAMINATIONS. I. W. BLUMENBERG, Beitr. z. klin. Tuberk. **62**:532, 1925.

A detailed report is made on postmortem examinations on 2,722 children up to 14 years of age with reference to tuberculous changes. A group of 163 cases was examined by the author, by hardening the organs in toto and sectioning them into 3 mm. thick slices. Of this group, seventy-five children (46 per cent) showed tuberculous foci. Of thirty-nine tuberculous children the tuberculin test was negative ten times. In four tuberculin positive children a thorough macroscopic and histologic examination did not reveal any tuberculous changes. In 61.3 per cent of the author's group, the primary infection was in the lung. All the extrapulmonary primary foci were abdominal. In the order of frequency the primary focus was located in the right upper lobe (36.2 per cent), left upper lobe (24.8 per cent), right lower lobe (19.7 per cent),

left lower lobe (15.7 per cent), middle lobe (12.6 per cent). In one third of the cases the primary focus was found to touch the pleura; in the other two thirds it was most always only 2-10 mm. below the pleura. Histologically, the primary pulmonary focus is a caseous hepatization, encapsulated, without the formation of tubercles; it is mostly solitary, and is frequently changed into a cavity, particularly in infancy. An ascending infection of the cervical lymph nodes does not occur; in every case of cervical lymph node tuberculosis, a focus along the upper respiratory tract can be demonstrated. The regional lymph glands were found to be caseated the more the younger the child was. Complete caseation occurred in 95.8 per cent during the first year, and 27.7 per cent between the 10th and 14th year. Secondary intestinal tuberculosis was present in 39.8 and 56.5 per cent, respectively. Tuberculosis of the tonsils and of the larynx was found only in intestinal tuberculosis. Bone tuberculosis was never found in infants. In one fourth of the patients with primary abdominal focus, no lesion was detectable in the intestinal mucosa; the author believes that tubercle bacilli may pass the intestinal wall without producing any pathologic changes in it (primary tuberculosis of the mesenterial lymph nodes). Intestinal primary foci are in contradistinction to the pulmonary ones multiple, as a rule. The prognosis of the primary mesenterial tuberculosis is good, that of the primary intestinal tuberculosis is poor.

The most frequent form of thoracic tuberculosis between 14 and 20 years of age is the chronic pulmonary tuberculosis with tubercle formation in the regional lymph glands. A previous, healed tuberculosis is rare, and has apparently no influence on a tuberculosis in this age group.

MAX PINNER.

THE PRESENCE OF CHILDREN NOT SENSITIVE TO TUBERCULIN IN FAMILIES WHERE TUBERCULOSIS EXISTS. RICHARD ZIMMERMANN, Ztschr. f. Kinderh. **39**:692, 1925.

Instead of looking at the high percentage of human beings who are sensitive to tuberculin, the author prefers to consider the number of people who are not sensitive. In thirty-three families observed by him, in each of which there was a case of tuberculosis, forty-five out of eighty-two children gave negative tuberculin tests, and they may have been for years under conditions of great exposure. Known cases of tuberculosis ordinarily are well guarded against, but this is not true of the coughs of some old people, or of light cases of tuberculosis, which are not recognized as such. The important thing is not the size of the dose of the infection, but the strength of resistance of the child. He wishes to point out that because mankind is susceptible to tuberculosis, it does not follow that infection may be an easy matter.

EMERSON, Boston.

ROENTGEN-RAY TREATMENT OF GLANDULAR TUBERCULOSIS. P. AMUNDSEN, Norsk. Mag. f. Lægevidensk. **87**:119, 1926.

The author has treated 150 patients suffering from glandular tuberculosis with roentgen rays, and kept them under control for from two to nine years after treatment. He observed a cure in 66 per cent of the cases, and thinks that this treatment ought to be tried in all cases of glandular tuberculosis. Relapse was seen in 4 per cent. One annoying complication was cutaneous changes, which were observed in 10 per cent. If the roentgen-ray treatment is continued for years, it is nearly impossible to avoid the occurrence of

cutaneous changes. The author advises that the irradiation of each series be distributed over several days, and an interval of five to six weeks between the different series elapse.

TOVERUD, Oslo, Norway.

Internal Diseases

FURTHER OBSERVATIONS ON THE ROENTGEN DIAGNOSIS OF BRONCHIECTASIS. ALEXANDER B. MOORE and WILLIAM J. MARQUIS, Am. J. Roentgenol. **13:** 527 (June) 1925.

The types are the infiltrative, or linear, cylindric and sacculated, representing different stages in the progress of the disease in the roentgenogram. The linear, characterized by an increase in the linear markings along the terminal bronchi, is usually localized in the lower lobes. The cylindric type is characterized by a greater density along the bronchi, fan shape in appearance and interspersed with clearer areas (dilated bronchioles, giving the appearance of cavities). These are more distinct after emptying the respiratory tract (Trendelenburg). The third, or sacculated type, represents the most advanced stage of the disease and is roentgenologically characterized by large pseudocavitations and a marked increase in the fibrous elements of the bronchial tract. In this stage, the usual involvement of the pleura may simulate a chronic empyema. There is probably an increased incidence due to massive pulmonary changes incident to recent influenzal epidemics, the use of irritative gases in warfare, the more frequent aspiration of foreign bodies, and the pulmonary fibrosis produced by intensive radiotherapy. Since symptoms may be extremely indefinite, the roentgenogram is valuable in establishing a diagnosis and a method of treatment.

STULIK, Chicago.

HEPATIC CIRRHOSIS IN CHILDREN. F. J. POYNTON and W. G. WYLLIE, Arch. Dis. Child. **1:1** (Feb.) 1926.

The entire subject of hepatic cirrhosis is presented, with a study of four unusual examples. In 5,500 necropsies at the Children's Hospital, Great Ormond Street, there were forty-eight cases of cirrhosis of the liver. The types are classified as:

1. Multilobular (portal, "hobnail", or "alcoholic").
2. Syphilitic (pericellular).
3. Type associated with Wilson's disease.
4. Type associated with icterus gravis neonatorum.
5. Hepatic cirrhosis in Banti's disease.
6. Type sometimes found in combination with "red atrophy" of the liver.
7. The biliary cirrhoses including hypertrophic biliary cirrhosis (Hanot), congenital cirrhosis, with or without obliteration of the bile ducts, and obstructive biliary cirrhosis.

The incidence of the types is given as: Type 1, 3 cases; type 2, 19 cases; type 3, 0 case; type 4, 0 case; type 5, 1 case; type 6, 1 case, and type 7, 24 cases. The various types are described in detail and are excellently illustrated. The special features of hepatic cirrhosis in the young are: the familial tendency, coexistent infantilism, and tendency to hemorrhage.

EPINEPHRINE IN SEVERE RHEUMATIC HEART BLOCK. G. A. SUTHERLAND, Arch. Dis. Child. **1**:21 (Feb.) 1926.

Sutherland cites an unusual case of severe rheumatic heart block successfully treated with epinephrine. The Stokes-Adams syndrome occurred about twenty-four hours before the arthritis symptoms and responded promptly to medication with epinephrine.

RECENT ADVANCES IN THE DIAGNOSIS AND TREATMENT OF PURPURA HEMORRHAGICA. BRUCE WILLIAMSON, Arch. Dis. Child. **1**:39 (Feb.) 1926.

Nothing new is added in this review of the published cases of purpura hemorrhagica. Only fifty-eight of the eighty-one reported cases in the literature are mentioned. It is well to remember that, in 1915, A. F. Hess first advised splenectomy in the thrombocytopenic type. There have been only two cases of splenectomy for this disease reported in Great Britain. The disease is probably not recognized.

KETONURIA AND URINARY ACIDITY. KENNETH H. TALLERMAN, Arch. Dis. Child. **1**:50 (Feb.) 1926.

It has long been observed that children may show acetone and diacetic acid in the urine following general anesthesia, and yet suffer no ill effects. Tallerman discusses the significance of ketosis without acidosis. The average urine *p*H of forty-two cases was 5.86, as determined by the well-known indicator methods. He feels that the ketone bodies may have a harmful effect.

PETERMAN, Milwaukee.

HYPERNEPHROMA OF THYROID, WITH CLINICAL PICTURE OF EXOPHTHALMIC GOITER. ANATOLE KOLODNY, Arch. Path. & Lab. Med. **1**:37 (Jan.) 1926.

The author reports the case of a woman who had had a goiter since the age of 15. At 68, she began to develop a typical picture of exophthalmic goiter, and on admission to the hospital, four months later, her basal metabolic rate was "plus 80." Bilateral subtotal lobectomy was performed, and the tissue removed showed multiple, circumscribed, opaque, yellowish white nodules, which, on microscopic examination, proved to be a typical reproduction of the cortical tissue of the suprarenal glands; a diagnosis was made of metastatic hypernephroma of the thyroid. Owing to the rarity of this condition, only one other case being found in the medical literature of the world, sections of the tumor were submitted to several prominent pathologists, who, with one exception, concurred in the diagnosis.

The author gives two possible interpretations for the occurrence of these nodules: one, that they were an overgrowth of aberrant suprarenal tissue in the thyroid, the other, that they were metastases from a hypernephroma. He considers the latter the more probable, because the former is found seldom in later life, and in all known cases of aberrant suprarenals the tissue was found below the diaphragm. Careful examination of the patient did not disclose the presence of a primary tumor.

PEARSON, Philadelphia.

CHLOROMA: THE RECENT LITERATURE AND A CASE REPORT. DORSEY BRANNAN, Bull. Johns Hopkins Hosp. **38**:189, 1926.

Chloroma or chloroleukemia is a myelogenous process—an unusual form of myelogenous leukemia. Aleukemic stages of chloroma are common, whereas

proved, true aleukemic forms of the disease are rare. Transitional or borderline and atypical cases occur, which emphasize the close relation between myelogenous leukemia and chloroma.

A classical case of chloroma is described.

AUTHOR'S SUMMARY.

THYMUS AND THE TREATMENT OF ITS HYPERFUNCTION. LAWRENCE R. DE BUYS, ERNEST C. SAMUEL and ELEAZAR R. BOWIE, J. A. M. A. **85**:1551 (Nov. 14) 1925.

The authors give their experiences with the roentgenography and radiotherapy of thymic hyperfunction. After studying the thymus shadow at frequent intervals from birth into the second and third years, they state that they are unable to arrive at a definite standard as to size, shape and position of the gland causing symptoms. Of a total of 623 children irradiated at different ages from birth to 39 months, 125 cases of thymic enlargement have been observed, or approximately 20 per cent. They have used both radium and the roentgen ray in treating these children, and have observed no ill effects with either. The average number of radium treatments necessary were three or four, while the number of roentgen-ray treatments required were four or five. The necessity for control of these cases has extended longer than a period of six months in only about one third of the cases.

BONAR, Salt Lake City.

STUDIES ON BACTERIAL (INFECTIVE) ENDOCARDITIS. WILLIAM S. THAYER, Johns Hopkins Hosp. Rep. **22**:1, 1925.

A monographic clinical and anatomic study of 198 instances of bacterial endocarditis. The concluding observations are:

"Various recognized infectious agents, among which Streptococci, Staphylococcus aureus, Pneumococcus, Gonoccocus and the Influenza group are the commonest examples, give rise, more or less frequently, to focal endocardial disease, verrucous, vegetative or ulcerative, valvular or mural endocarditis, associated sometimes with acute, often suppurative pericarditis, and focal, often suppurative myocarditis. The endocardial lesions are, as a rule, the most important.

"Bacterial disease of the heart ('malignant' or 'infective' endocarditis), may be divided into two main forms: 1. In the first, the lesions appear commonly as complications or sequels of some focal inflammatory process with an accompanying septicaemia which is usually rapidly fatal. Under such circumstances the existence of cardiac disease is generally masked by the symptoms of the acute infection of which it is a complication. In peracute cases the lesions are verrucous, scarcely larger than those of rheumatic heart disease. In those with a course of several weeks the changes are usually vegative or ulcerative. In most acute septicaemias the cardiac disease is clinically subsidiary to its mother infection—a mere incident in an acute septicaemia or pyaemia.

"2. In other instances especially in infections with attenuated streptococci, notably *Streptococcus viridans*, and with *B. influenzae*, the endocardial focus is truly the main seat of the disease. The course of the malady is slow, subacute or chronic, lasting over weeks and months. The onset is insidious; the portal of entry is obscure; and the areas involved are generally the seat of previous chronic rheumatic disease. The manifestations are rather those of subacute or chronic septicaemia to which later the characteristic embolic phenomena are added. Here the subacute endocarditis is in itself the essential pathologic entity.

"While rheumatic heart disease is a true pancarditis, these recognized bacterial affections of the heart may be and often are, essentially or purely, endo-, peri, or more rarely, myocardial. The infrequency of extensive myocardial change is striking.

"With recovery which apparently is not very frequent, there remain deformed, sclerotic or calcified valves, or perhaps, an adherent pericardium or myocardial scars. But recovery is apparently relatively unusual.

"Syphilis is an important cause of disease of the aorta and often affects the aortic valve with resultant aortic insufficiency and its consecutive changes. It is probably associated with grave myocardial disease more commonly than is generally appreciated.

"Rheumatic fever and chorea stand together as manifestations of that infection which is associated with those peculiar acute cardiac changes which we have come to class as 'rheumatic.' The so-called 'rheumatic' cardiac lesions affect the entire heart. They consist of the peri-vascular Aschoff bodies, the frequent sero-fibrinous pericarditis, the slowly developing and cicatrizing valvulitis and verrucous endocarditis, notably of the mitral orifice. These processes terminate in the familiar picture of chronic valvular disease of the heart with disseminated peri-vascular fibrosis of the heart-muscle, and often with adherent pericardium.

"The acute infections, other than rheumatic fever and chorea and syphilis, appear to play a small part in the production of chronic valvular disease of the heart."

[ARCH. PATH.]

CLINICAL STUDY OF 221 OPERATED CASES OF HYPERTROPHIC CONGENITAL PYLORIC STENOSIS. ISAAC A. ABT and ALFRED A. STRAUSS, M. Clin. N. Amer. **9**:1305 (March) 1926.

The experience of the authors in the diagnosis and treatment of 221 cases of hypertrophic congenital pyloric stenosis, for which operations were performed, is summarized in this paper.

The percentage of males was high, 161 out of the total number. Breast feeding had been practiced exclusively in 119; 101 had received some complementary feeding, and only one was fed artificially with no breast milk.

Vomiting, the outstanding symptom, appeared most frequently during the second or third week of life, and was characteristically projectile. Peristaltic waves were observed in all cases after taking milk from the breast or water from a bottle. Tumor was definitely palpable in 25 per cent of the cases.

On fluoroscopic examination after the ingestion of a small amount of barium in breast milk, "rhythmic, snake-like, peristaltic contractions seen in the pylorus, independent of the rest of the stomach, are absolutely pathognomonic of the condition." If one-half or more of the barium meal remains in the stomach after four hours, the subject is referred for operation. When 80 per cent or more passes the pyloric in four hours, operation is deferred. A large dilated stomach was noted in all subjects more than 4 weeks old.

Preoperative treatment consisted of salt solution by hypodermoclysis, and glucose and sodium bicarbonate by rectum. When the condition was very poor, glucose solution was given via the superior longitudinal sinus, usually followed within six hours by the transfusion of from 60 to 80 cc. of blood.

The Strauss pyloroplasty was done in all cases. In forty-eight the tumor was small, and no flap was made. A tumor was invariably found at operation, which contracted and relaxed rhythmically. The size of the tumor was

in direct proportion to the age of the child, or the length of time elapsing since the onset of the symptoms. Older babies had larger tumors than younger ones.

Feeding was started early, within an hour after operation, and consisted of 1 drachm (4 cc.) of breast milk every two hours, gradually increased. Vomiting was more frequent in those in whom no plastic flap was made.

Seven patients died, a mortality of slightly over 3 per cent. Two came to the hospital moribund; one died of peritonitis; two of an intercurrent influenzal pneumonia, and one had multiple atresias of the intestinal tract.

The authors conclude that early surgical treatment in well defined cases of pyloric stenosis offers the safest and most certain method of treatment.

A Case of Purpura Hæmorrhagica. Full Discussion of Blood Findings and Clinical Features. Charles Spencer Williamson, M. Clin. N. Amer. **9**:1353 (March) 1926.

In differentiating scurvy from purpura hemorrhagica, the point is made that the characteristic features of the gums in scurvy are sponginess and stomatitis and not bleeding. In scurvy also there is generally found the so-called scurvy sclerosis, the result of hemorrhages into the great muscle masses. In purpura hemorrhagica, besides the spontaneous hemorrhages in the skin and mucous membranes, there may be bleeding from the uterus, stomach, bowels and kidneys. Subcutaneous hemorrhages as a result of slight trauma are of frequent occurrence. The characteristic laboratory findings are anemia with an approximately normal color index, diminished platelets, prolonged bleeding time with near normal coagulation time, and a soft nonretracted clot. The prothrombin test of Howell may give valuable information. It consists in the determination of the point at which oxalated blood serum is coagulated on the addition of 0.5 per cent solution of calcium chloride, using normal serum as a control.

The only form of treatment which promises anything is blood transfusion. Frequent intramuscular injections may be used instead, which bring about at least a transitory increase of the platelets.

Smith, Ogden, Utah.

The Mediastinum as a Focus of Infection. W. L. McClure, Northwest Med. **25**:36 (Jan.) 1926.

McClure says the mediastinum and adjacent structures may act as a definite focus with resulting toxemia and bacteriemia, and that by careful study, especially with the fluoroscope, this focus can be recognized. He believes the *Staphylococcus aureus* in this locality plays as important, if not more important, rôle than the streptococcus.

Tenia Saginata. A New Method of Treatment. J. Shelly Saurman, Northwest Med. **25**:42 (Jan.) 1926.

Saurman avoids the nauseous taste of the teniafuge by administering it through a duodenal tube. A preliminary fast with saline enemia are ordered, and the patient comes to the office in the morning. The tube is passed and 2 cc. of oleoresin of aspidium is introduced in quite warm water. Following this 100 cc. of 33 1/3 per cent magnesium sulphate is injected. In the case cited a 22 feet long tapeworm, with head intact, was passed eighty-five minutes after the aspidium was given and the patient was able to return home a few minutes later.

STRICTURES OF THE ESOPHAGUS—METHODS OF RECONSTRUCTION OF THE ESOPHAGEAL LUMEN. PAUL W. SPICKARD, Northwest Med. **25**:90 (Feb.) 1926.

Spickard reviews the literature on this subject, with special regards to methods of treatment by dilatation and esophagoplasty. A bibliography is appended. The reader is referred to the original article.

SCOTT, Philadelphia.

ACUTE HEMORRHAGIC NEPHRITIS IN CHILDREN. W. G. WYLLIE and ALAN MONCRIEFF, Lancet **1**:128 (Feb.) 1926.

An analysis of eighty-seven patients with nephritis, admitted to the Great Ormond Street Hospital during three years, were divided as follows:

Acute nephritis	23	Chronic nephritis	42
Acute hemorrhagic nephritis	22	(a. Chr. parenchym. neph	23)
		(b. Chr. interstit. neph	19)

Acute Parenchymatous or Exudative Nephritis.—This is characterized by general edema, headache, vomiting, a rise in temperature, a reduction in the quantity of urine, which is albuminous to a degree exceeding that accountable for by the amount of blood which may be present during the period of oliguria. Large numbers of casts of all varieties are found and the blood pressure is often raised.

Acute Hemorrhagic Nephritis.—This is more benign. Blood occurs in the urine quite suddenly, sometimes during, but usually a few days after, some acute or subacute infection of the nasopharyngeal region, and may continue to be passed in smaller quantities for several days or weeks. Edema is slight if it occurs. The urine is little if at all reduced in quantity and contains a large quantity of blood, often remaining red or smoky for several days. Usually the casts are few and as a rule there is no rise in blood pressure.

Etiology.—Streptococcus infections, the commonest precursors of acute nephritis in children. Staphylococcus and pneumococcus may also be responsible. Tonsillitis with or without accompanying otitis media is by far the commonest cause.

Twenty-two cases of hemorrhagic nephritis are analyzed: ten boys and twelve girls. The authors suggest that pathologically it is probably a form of streptococcal embolism of the kidney, originating from some definite focus of sepsis elsewhere in the body.

The prognosis is much better than in the other forms of acute nephritis, and as a rule no chronic infection of the kidney results.

LANGMANN, New York.

CARDIAC INFANTATION. I. RISIEN RUSSEL, Proc. Roy. Soc. Med. (Section for the Study of Disease in Children) **19**:3 (Nov.) 1925.

I. Risien Russel presented a case of cardiac infantilism in a boy, aged 15 years. The family history was negative, and the past history up to this age was negative except it was noticed his skin very easily turned blue, and at school he was unable to play games, to run about or climb stairs. At this age the patient showed distinct infantilism, his height being 4 feet 1 inch and his weight 52 pounds. He also showed typical signs of congenital heart disease. A roentgenogram showed distinct enlargement of right ventricle, and also of the bulbus cordis. Mentally, the boy was very alert.

LYMPHOCYTIC LEUKEMIA? HUGH THURSFIELD, Proc. Roy. Soc. Med. (Section for the Study of Disease in Children) **19**:4 (May 22) 1925.

Thursfield reported a case of a boy, age 4½ years, who was in good health till January of this year when glands in neck and axilla commenced to enlarge, and the mouth was inflamed and ulcerated. On admission to the hospital, on January 23, he was anemic with purpuric spots on his back. Cervical, axillary, submaxillary glands were enlarged, firm, discrete and painless. There was a hard, rounded painless swelling beneath the scalp. The liver was freely movable; the spleen was enlarged. Red cells, 3,200,000; white cells, 7,800, 96 per cent of which were lymphocytes. Blood platelets per cubic centimeter were normal. During the following two months, the child grew progressively worse. Epistaxis and edema occurred, fluids were sometimes regurgitated through the nose and the patient was almost aphonic. The white blood cells had fallen to almost 1,000 per cubic centimeter.

At the end of March, a gradual improvement commencd. On March 27, the right ear began discharging profusely, and streptococci were isolated. In May, the red cells were 5,040,000; white cells, 10,000; 61 per cent lymphocytes; the submaxillary glands were still palpable and the right side of the face was swollen. When last seen, on May 19, 1925, several hard painless lumps were palpable in the scalp and a small sequestrum of bone had separated from the posterior part of right half of the mandible. The patient appeared to be in fairly good health.

1. Is this a case of lymphocytic leukemia which has reached a stage of quiescence?

2. If not, is it conceivably such a case as is reported from time to time, in which suppuration instead of polymorphonuclear leukocytosis produces a lymphocytic reaction?

3. What are the lumps on the head?

Note: This patient died on June 16, and the diagnosis of lymphocytic leukemia was confirmed at necropsy.

WILLIAMSON, New Orleans.

TREATING OF SUPPURATING INFLAMMATIONS BY FILTRATE ACCORDING TO THE METHOD OF BESREDKA. N. N. BOURDENKO and N. L. GIVAGO, Ann. de l'Inst. Pasteur **60**:232 (March) 1926.

This method of treatment for suppurating wounds consists in isolating the predominating organism and transplanting it into bouillon. After about eight hours of incubation, it is filtered through a porcelain filter, the p_H of the medium is adjusted to about 7.2, and it is then reinoculated with fresh cultures of the same organism. This procedure is repeated until the organism will no longer grow in the medium. Then the latter is filtered through a porcelain filter, and applied locally to the lesions by means of compresses, tampons or irrigation.

The authors render animals immune to invasion of various types of organisms by swathing them in compresses soaked in medium prepared as in the foregoing. Only bouillon from homologous strains offered this protection.

This method was used in the treatment of a variety of suppurative conditions of bones, joints and skin, may of which had resisted all other types of treatment. Their results were very prompt, and were characterized by increase of circulation at the site, diminution of discharge, and rapid healing. Eighty

per cent of the cases treated showed marked improvement, both local and general. No secondary phenomena were associated with its use. Autofiltrates are much more effective than stock filtrates.

BOYD, Iowa City.

CONTRIBUTION TO THE CHEMISTRY OF THE BLOOD OF CARDIAC PATIENTS. CALCIUM AND CARDIAC TONE. BEHAVIOR OF THE CALCIUM IN THE BLOOD. A. GALLUPPI, Arch. di pat. e clin. med. **4**:577, 1925.

The author determined the calcium content of the blood in thirty patients with various forms of heart disease, but was able to find no relation between the symptoms or diagnosis and the calcium content of the blood serum. In the same person, however, the calcium content of the blood was found to be higher when the heart was compensating than when it was decompensating.

The author gave 10 per cent calcium chloride intravenously with very good results to patients with acute dilation of the heart, combining this treatment with such drugs as digitalis, caffeine, quinine and strychnine. Calcium chloride is contraindicated when there is a "tonic constriction of the heart."

HIGGINS, Cincinnati.

INTESTINAL NECROSIS DUE TO ASCARIS. K. TAKEUCHI, Virchows Arch. f. path. Anat. **258**:502, 1925.

Takeuchi reports a case of fatal peritonitis in a 5 year old child, due to perforation of the intestine. In addition to the perforation there were numerous areas of sharply circumscribed necrosis in the intestinal wall, which involved the entire thickness of the wall and which were suggestive of pressure necrosis because of the absence of reactive phenomena in the tissue. Pressure by the large convoluted masses of *Ascaris* present was not believed, however, to be the chief factor in the necrosis, the action of toxins being considered more important.

O. T. SCHULTZ.

THE WATER ECONOMY IN CHILDREN WITH MYXEDEMA. E. NOBEL and A. ROSENBLUTH, Ztschr. f. Kinderh. **39**:702, 1925.

The authors made a complicated estimation of the insensible perspiration, based on the food intake, urine and stool output and daily fluctuation of the body weight, and concluded that the dry condition of the skin found in myxedema is due to an apparent diminution in the insensible perspiration.

STUDIES IN MYXEDEMA. 6. QUANTITATIVE THERAPY IN MYXEDEMA BASED ON CLINICAL OBSERVATIONS OF A YEAR'S DURATION. E. NOBEL and A. ROSENBLUTH, Ztschr. f. Kinderh. **39**:708, 1925.

This article deals with the importance of standardized preparations of thyroid gland and gives a practical table of dosage.

EMERSON, Boston.

CHRONIC ABDOMINAL PAIN IN CHILDREN. KIRSTEN UTHEIM TOVERUD, Norsk Mag. f. Lægevidensk. **87**:119, 1926.

The author has observed eighty children, aged from 4 to 14 years, in whom the predominant symptom was recurrent abdominal pain with general malaise, headache, poor appetite and irritability. All these children were suffering from more or less severe constipation, and when this constipation was treated, the

other symptoms, together with the recurrent pain, completely disappeared. The author thinks that chronic constipation in children is an important factor in producing the picture of what is called intestinal colic or intestinal indigestion in the textbooks. The causes for the constipation in these children were mostly a poorly composed diet and bad habits. A change of the diet to the so-called "constipation diet", consisting of much vegetables, fruit, lactic acid milk, whole wheat bread with some meat, effected a cure. No medicines were used at all. In a few severe cases abdominal massage was employed.

TOVERUD, Oslo, Norway.

Nervous Diseases

THE EFFECT OF THE SYMPATHETIC NERVOUS SYSTEM ON THE PERIPHERAL VASCULAR SYSTEM. W. B. MOSSER and K. P. A. TAYLOR, Arch. Surg. **72**:760 (March) 1926.

Using the temperature of the limb as an indicator, these authors found no appreciable change following periarterial sympathectomy. By injecting alcohol into the sciatic nerve in sufficient strength to cause motor paralysis, they produced a rise in temperature averaging 4.5 degrees, which subsided as motor function returned.

N. ENZER.

OBSTETRIC PARALYSIS. JAMES WARREN SEVER, J. A. M. A. **85**:1862 (Dec. 12) 1925.

The author reports 1,100 cases of obstetric paralysis. The right arm was affected 670 times, and the left 430, or about 64 per cent in favor of the right arm. Upper arm paralysis was most frequent, occurring 829 times, while the so-called lower arm or, better, whole arm type, occurred 208 times. In sixty-three cases both arms were affected, the whole arm type being the least common. It is generally acknowledged that a difficult and prolonged labor is a predisposing factor of the greatest importance in the causation of this paralysis. In this series, 589 of the deliveries were long and difficult, and, in a large proportion forceps were used. Most of the mothers had ether, which presupposes a relaxed and asphyxiated child. While the foregoing conditions imply application of force combined with great muscular relaxation in the child, a moderate number had a normal labor. There were 443 head or face presentations. These figures show the much greater frequency of vertex presentations in relation to both types of paralysis. First babies make a harder entrance into this world than those that follow, and the paralytic conditions seem to exist more with them than with later babies. The author states that splints may be used but favors operative treatment. Operations designed to relieve muscle contractures are undertaken freely, as a rule not later than at the age of 4 or 5 years, and by division of the contracted muscles, it is possible to give the child a much better arm, not only from a cosmetic but a functional point of view. The author's operation is described. If the babies can be seen early, later operations may be prevented, and in the upper arm type, fairly good functional arms may be obtained, with the exception of the ability to supinate normally. In old untreated cases operation is necessary. The treatment should be begun immediately and should be carried out faithfully for years under the eyes of a physician, masseur or nurse. The arm when first seen should never be put in a sling or a Velpeau bandage, but should be either left entirely free with the other arm pinned, or should be put on a splint.

BONAR, Salt Lake City.

THE EFFECT OF THE ADMINISTRATION OF CALCIUM SALTS AND OF SODIUM PHOSPHATE ON THE CALCIUM AND PHOSPHORUS METABOLISM OF THYROPARATHYROIDECTOMIZED DOGS, WITH A CONSIDERATION OF THE NATURE OF THE CALCIUM COMPOUNDS OF BLOOD AND THEIR RELATION TO THE PATHOGENESIS OF TETANY. ISIDOR GREENWALD, J. Biol. Chem. **67**:1, 1926.

The author presents the hypothesis that the calcium of the plasma exists in two forms; (1) inorganic calcium, largely as calcium phosphate, and (2) organic calcium, resembling but not identical with calcium citrate. Parathyroid hormone is necessary for the preparation in the body of the organic calcium.

HIGGINS, Cincinnati.

DEMENTIA PRAECOX IN IDENTICAL TWINS. G. H. PARKER, J. Nerv. & Ment. Dis. **63**:135 (Feb.) 1926.

The author reports a case of female twins who had been inmates of the McLean Hospital with a condition diagnosed as dementia praecox. Both had had diphtheria at the age of 16. At the age of 20 both were admitted to hospital with acute excitement, one after a gradual neurasthenic onset, the other with quite sudden onset. For thirty-three years they were patients in separate hospitals. In the protracted phase of their psychosis both talked incoherently, muttered to themselves, showed no power of attention or interest in anything and were subject to impulsive outbursts of noise and destructiveness. After their long separation they met at the McLean Hospital, and there showed striking similarity in behavior and reaction picture. The author declares that there are two kinds of twins, those from a single ovum and placenta — these he calls identical twins and says they are always of the same sex; and those from different ova, protected with separate fetal membranes — these may be of the same or opposite sex. Leeman discovered seventeen recorded instances of dementia praecox in twins; study of these cases helps to distinguish between traits due to germinal inheritance and those due to environmental influence. The simultaneous occurrence of dementia praecox is strongly in favor of a germinal source for this disease.

HART, Philadelphia.

THE SYNDROME OF COMPRESSION OF THE SPINAL CORD. HENRY W. WOLTMAN, Northwest Med. **25**:17 (Jan.) 1926.

Woltman reviews the essentials of spinal physiology and diagnosis. Localization by examination of reflexes, of sensation, by the results of spinal puncture, by roentgen ray, and by a carefully taken history are discussed. The diagnosis of cord tumors from other spinal diseases is considered. Woltman concludes: (1) that a stubborn pain for which no explanation can be made may be a root pain; (2) that a gradually increasing loss of motion and sensation below a definite level suggest a cord tumor; (3) that 57 per cent of cord tumors are removable and that 42 per cent of patients are completely cured.

EPIDEMIC ENCEPHALITIS. R. M. BOWELL, Northwest Med. **25**:25 (Jan.) 1926.

Bowell gives a résumé of the history, etiology, pathology, symptoms, differential diagnosis and treatment of epidemic encephalitis. No case histories are reported.

SCOTT, Philadelphia.

PROTEIN SENSITIZATION IN EPILEPSY—A PRELIMINARY REPORT. J. FRANCES WARD and HAROLD A. PATTERSON, State Hosp. Quart. **10**:429 (May) 1925.

After a comprehensive review of the literature on protein sensitization, the authors conclude that a local inflammatory reaction may occur in the meninges of sensitized persons as well as anywhere else. Such a reaction could cause a swelling that would exert pressure on the sensory and motor centers and thus produce the well known symptoms of epilepsy. In this preliminary report, 100 epileptic patients were tested with group allergens. In 50 per cent of all cases tested there was a positive reaction; the preponderance of patients reacted to the fish group, the next greatest number to fowl and the third to vegetables. With the individual proteins about 50 per cent again showed a positive reaction. In this test the oat protein predominated, and lactalbumin was second and cauliflower third.

No therapeutic measures have yet been instituted, but the authors anticipate that a great deal can be accomplished toward reducing epileptiform seizures by determining the protein responsible for the irritation of the meninges.

HOWARD, Milwaukee.

A NEW METHOD OF DEMONSTRATING MEDIAN NERVE LESIONS. DENNIS CRILE, Surg., Gynec. & Obst. **43**:325, 1926.

Production of a passive hyperemia by means of a sphygmomanometer at diastolic pressure, will produce in the area supplied by the sensory fibers of a paralyzed peripheral nerve definite color changes in the skin as compared with the normal areas. After one minute, the area involved is reddened, instead of being mottled, after three minutes it is quite cyanotic, after five minutes very cyanotic and cold, and after twenty minutes extremely cyanotic.

This test is valuable because it cannot be feigned by a malingerer, and can be used in early cases before vasomotor changes resulting from the nerve lesion have taken place.

MILLER, Chicago.

A FAMILY WITH PROGRESSIVE FAMILIAL CEREBRAL (SO-CALLED CEREBRO-MACULAR) DEGENERATION. W. J. ADIE, Proc. Roy. Soc. Med. (Section for the Study of Disease in Children) **19**:1 (Nov.) 1925.

Dr. Adie showed four patients from one family suffering from familial cerebromacular degeneration, the onset of symptoms occurring during the seventh year of life, with slow mental deterioration, convulsions, visual failure with optic atrophy and retinal degeneration, progressive spastic weakness of the muscles and curious involuntary jactitations. The two youngest in the family are still healthy with normal fundi.

This disease presents itself in several more or less distinct forms, the most familiar being the amaurotic family idiocy, the infantile type, beginning in the early months of life characterized by progressive loss of muscular power, progressive visual failure, with the typical cherry-red spot at the macula, rapid dementia and death within a year or so. The form exhibited by the before-mentioned family is known as the juvenile type. The course is slower, the triad (paralysis, loss of vision and dementia) is fairly constant. There is no cherry-red spot at the macula but a retinitis pigmentosa beginning in the macular region or optic atrophy.

A third form, the late infantile type of Jansky and Bulschowsky, appears about the third year and ends in death in three or four years.

In any of the three types, one of the cardinal signs may be absent. The only constant feature of the disease is the peculiar histologic change just described by Schaffer in the ganglion cells and their dendrites, the cells being of enormous size, and a peculiar lipoid pigment seen within them. Any part of the brain may be spared. A feature noticed in many of the cases was the small size of the cerebellum.

True Narcolepsy Onset at the Age of Twelve Years. W. J. Adie, Proc. Roy. Soc. Med. (Section for the Study of Disease in Childhood) **19**:2 (Nov.) 1925.

The author reports a case of true narcolepsy, which was first diagnosed as minor epilepsy. The patient had attacks in which she simply fell asleep, and in them presented every appearance of normal sleep. She had another interesting symptom—if she laughed heartily, she had difficulty in standing, sometimes she would fall down. The author had seen four other cases of true narcolepsy presenting this symptom. The name, narcolepsy should be applied to conditions in which attacks of natural sleep of short duration occur in otherwise healthy persons. In textbooks, it is described as a disease of adult life—the youngest case on record is that of a youth aged 18 years.

A Family Afflicted with Amyotonia Congenita. W. J. Adie, Proc. Roy. Soc. Med. (Section for the Study of Disease in Childhood) **19**:2 (Nov.) 1925.

The author presented five members of a family of thirteen children, all of whom showed well the characteristic features of amyotonia congenita. One of these is a tendency to progressive improvement.

Williamson, New Orleans.

Postdiphtheritic Hemiplegia. Hinds Howell, Proc. Roy. Soc. Med. (Section for the Study of Disease in Children) **19**:3 (Nov.) 1925.

The patient presented had suffered from a severe attack of diphtheria five years previously, with hemorrhage from the nasopharynx and bowels, and hematuria. Tracheotomy had been performed. The attack left paralysis of accommodation, palatal paralysis and right hemiparesis. The ocular and palatal paraylsis have disappered, but the hemiparesis remains, accompanied by writhing athetosic movements of the right arm and leg. This kind of case differs from all other varieties of diphtheritic paralysis, in that the damage of the nervous system is secondary to changes in the blood vessels, embolism, thrombosis or hemorrahagic encephalitis. The author believed this case was one of hemorrhagic encephalitis. Hemiplegia as a residue of diphtheria is extremely rare.

Microcephalic Idiocy as a Result of Traumatic Birth Injury. S. Schmal, Ztschr. f. Kinderh. **39**:732, 1925.

The author reports three cases, one of them with necropsy, and suggests that microcephalic idiocy may be secondary to traumatic birth injury.

Emerson, Boston.

Diseases of the Ear, Nose and Throat

INFANTILE OTITIS MEDIA. DANA W. DRURY, Boston M. & S. J. **194**:96 (Jan. 21) 1926.

In view of the frequent association of ear infections in cases of infantile malnutrition and gastro-intestinal disturbances, this is a very timely, interesting and helpful article. The author explains clearly the physical aural conditions so conducive to infection in infancy, and cites and discusses various typical cases of otitis media occurring in the first year of life. The importance of early incision of the drum, especially in the infectious diseases, is emphasized; also the removal of adenoid tissue (without anesthetic) when it is a predisposing or complicating factor.

GENGENBACH, Denver.

ACUTE SUPPURATIVE OTITIS MEDIA. ARCHIBALD W. HOWE, Northwest Med. **25**:33 (Jan.) 1926.

Howe reviews the anatomy and physiology of the ear and the etiology, symptoms, diagnosis and treatment of otitis media. He advises the instillation of a 5 per cent phenol (carbolic acid) in glycerine, laxatives, external heat and rest in bed for those whose ears are red but not bulging. He advises early incision if the drum is bulging and follow up treatment by the dry method, that is, frequent wiping of the canal and the insertion of dry wicks. Ears discharging for an unduly long time are treated with suction and mercurochrome-220 soluble instillations.

SCOTT, Philadelphia.

SUPPURATIVE DISEASES OF THE LUNGS DUE TO INSPIRATED FOREIGN BODIES CONTRASTED WITH THOSE OF OTHER ETIOLOGY. CHEVALIER JACKSON, Surg. Gynec. Obst. **43**:305 (March) 1926.

It is surprising, and yet it is the rule, that, after bronchoscopic removal of a foreign body from the air passages, a suppurative process even of great extent and long duration will clear up without difficulty and the lung return to normal. It is the exception, however, for such results to follow suppuration when due to other causes. The character of the suppurative process in the lung when due to a foreign body varies a great deal, depending on the type of foreign body and the degree of obstruction produced in the bronchus. A peanut kernel in the air passage often sets up a suppuration that may be fatal in a short time, when a screw or tack may be present in the lung for many years without producing much reaction or causing noticeable disability. In fact, the metallic foreign bodies seem to have a germicidal action that holds suppurative processes in check unless complete obstruction to the passage of air has taken place. A bronchiectasis under ordinary conditions is a most obstinate thing to treat and the prognosis is usually bad, but when secondary to an abscess produced by a foreign body, the condition almost always clears up without difficulty after removal of the etiologic factor.

The explanation of these clinical phenomena is not easy, but it may be in the fact that, when a foreign body with its surrounding granulation tissue is once removed, the obstruction is permanently relieved, whereas when a post-pneumonic, or embolic abscess is drained bronchoscopically, the granulation tissue plug readily reforms and free exit of the pus is thus prevented.

MILLER, Chicago.

Diseases of the Skin

MICROCHEMICAL STUDIES OF ARSENIC IN ARSENICAL PIGMENTATION AND KERATOSES. EARL D. OSBORNE, Arch. Dermat. & Syph. **12**:773 (Dec.) 1925.

A method is described whereby arsenic is converted to the trisulphid in tissues, and thus becomes visible in tissue sections when examined microscopically. This method is applied in the study of a case of arsenic keratosis and one of arsenic pigmentation. Arsenic was noted in considerable quantity in all parts of the skin, the greatest deposit, particularly in the keratosis case, being in the basal layers of the epidermis and in the papillae of the corium. Most of the arsenic was in the intercellular spaces. It seemed probable that some was within the cells, but this was not certain.

THRUSH INFECTIONS OF THE SKIN. BEDFORD SHELMIRE, Arch. Dermat. & Syph. **12**:789 (Dec.) 1925.

The literature is reviewed and several cases are reported. In infants, thrush may become generalized and the infection may prove fatal. In older persons, the infection is most likely to occur in the body folds or in areas kept moist by wet dressings or the continuous bath. In the infant, "the primary efflorescences are superficially situated, pinhead vesicles which frequently become pustular, or lentil sized areas of erythema with branlike scaling in the central portions. The vesicles and pustules soon rupture, leaving behind small denuded areas, surrounded by a collar of undermined epidermis. These areas, as well as the initial small areas of erythema, extend peripherally to form small, coin sized erythematosquamous patches with elevated borders. Through confluence of smaller lesions, larger patches are formed."

JEANS, Iowa City.

SO-CALLED ACRODYNIA OR ERYTHREDEMA (SWIFT'S DISEASE). A. S. WARTHIN, Arch. Path. & Lab. Med. **1**:64 (Jan.) 1926.

Two cases of erythredema, studied pathologically by Warthin, showed essentially the following changes: extreme edema of the meninges and brain, with dilatation of the central canal of the spinal cord. There was proliferation of the meningeal and perivascular reticulo-endothelium, both in the nervous system and around a few of the peripheral nerve trunks. No degenerative or inflammatory changes were found either in the central nervous system or in the nerves. There was chronic erythema of the skin, with hyperkeratosis, hypertrophy of the epidermis and sweat glands, slight pigmentation of the rete and hypoplastic lymphatic constitution. There was associated or terminal respiratory infection, gastro-intestinal catarrh and inanition.

The changes in the skin and nervous system suggested the pathologic change of the early erythema stage of pellagra, and the skin changes were identical with those occurring in light sensitization and in certain stages of roentgen-ray and ultraviolet-ray erythemas. Warthin considers that the entire anatomic picture resembles that due to a food deficiency or a toxic state in persons of the hypoplastic constitution, affecting the reticulo-endothelial system of the meninges and skin, and the vegetative nervous system, and possibly leading to light sensitization.

PEARSON, Philadelphia.

CLINICAL CALORIMETRY. XL. THE EFFECT OF THE ABSENCE OF SWEAT GLANDS ON THE ELIMINATION OF WATER FROM THE SKIN AND LUNGS. HENRY B. RICHARDSON, J. Biol. Chem. **67**:397, 1926.

The subject of this study was a boy, aged 14, with congenital absence of the sweat glands, as proved by microscopic examination of the skin. Twenty-eight per cent of the heat produced was eliminated in the form of water vapor; approximately 30 per cent of the water vapor was excreted from the lungs, and the remainder from the skin; these figures are essentially normal. Even when the metabolism was increased to 250 per cent of normal, heat and water elimination were such as to maintain the body temperature normal. Exposure of the head to hot air did not cause increased elimination of the water vapor from the skin, and the body temperature rose; a similar experiment with a normal person led to profuse sweating.

Water is eliminated from the skin in other ways than through the sweat glands; the sweat glands seem to constitute an emergency apparatus, which is called on only under exceptional conditions.

HIGGINS, Cincinnati.

VON RECKLINGHAUSEN'S DISEASE OR NEUROFIBROMATOSIS. MORRIS L. BRIDGEMAN, Northwest Med. **25**:144 (March) 1926.

Bridgeman reports a case of Von Recklinghausen's disease in a boy aged 13, showing progressively enlarging swellings, apparently congenital, varying in size from that of a millet seed to that of an almond, along the course of the ulnar, radial and sciatic nerves, and over the chest, back, head and buttocks. Associated were brownish freckles and pigmentation. The boy showed retarded sexual characteristics, retarded mentality and nervousness, and had headache, rheumatic pains and night sweats.

SCOTT, Philadelphia.

CONTRIBUTION TO THE ETIOLOGY AND THERAPEUSIS OF ECZEMA. DOCENT DR. HUBSCHMAN, Cas. lek. cesk. **64**:244 (Feb.) 1925.

Intravenous injection of 10 per cent solution of sodium bromide in increasing daily doses of 2 to 10 cc. had a beneficial effect on an acute exacerbation of an adult, chronic eczema. The author feels that simultaneous local treatment is not essential. Samberger's idea of eczema is one of inflammation associated with hyperproduction of lymph. The unstable secretory reaction is due to changes in the capillary endothelium, or in the nervous mechanism concerned with the secretion.

STULIK, Chicago.

Surgery and Orthopedics

PES CAVUS. A. S. B. BANKART, Arch. Dis. Child. **1**:26 (Feb.) 1926.

Pes cavus without evidence of paralysis is quite a characteristic deformity. It is bilateral and makes its appearance in the latter part of childhood, coming on gradually without apparent cause. It is often hereditary and may occur in several members of a family. In three cases there were found: in one, a defect in the lamina of the fifth lumbar vertebra; in one, a diminution in size of the first sacral roots, and in another, a thickening of the the dura at the fifth lumbar and first sacral. Steindler's operation is advised.

FOUR CASES OF IMMUNOTRANSFUSION. E. L. LLOYD and B. E. SCHLESINGER, Arch. Dis. Child. **1**:54 (Feb.) 1926.

Immunotransfusion was considered a decisive factor in the recovery of one of four patients thus treated. All four patients showed positive blood cultures. The organism is isolated from the blood culture, and a vaccine is made and injected subcutaneously into a suitable donor. Five hours later the donor's blood is drawn, defibrinated and injected intravenously into the patient.

PETERMAN, Milwaukee.

BIRTH INJURIES REQUIRING ORTHOPEDIC TREATMENTS. SAMUEL W. BOORSTEIN, J. A. M. A. **85**:1866 (Dec. 12) 1925.

Many permanent injuries are traced to parturitional trauma. Many of these injuries can be diagnosed at birth if careful examination is made. The attending physician should be familiar with the proper methods of prompt diagnosis in order that early treatment can be instituted. If he is unable to diagnose the condition, he should consult an orthopedic surgeon. Spastic conditions should receive immediate treatment even when the child is mentally inferior. Cases of intracranial injury are treated by a double Thomas abduction frame with arm attachments. Obstetric brachial paralysis is best treated by a plaster or an abduction splint, keeping the arm in abduction and outward rotation. Later on, massage and exercises are instituted. Fractures of the femur and the humerus are treated with a small Thomas Jones splint. Fractures of the spine are treated by means of a Bradford frame. Torticollis is prevented by a felt collar around the neck.

BONAR, Salt Lake City.

EMPYEMA OF UNUSUAL ORIGIN. JESSE R. GERSTLEY, M. Clin. N. Am. **9**:1413 (March) 1926.

A girl, aged 15, had complained for some time of pressure behind the sternum, with sense of obstruction to the passage of food at this point. Later, some pain was experienced. Examination was negative except that the roentgenogram showed some narrowing of the lumen of the esophagus just above the cardia. On passage of the esophagoscope, slight resistance was felt, which immediately disappeared, but the child experienced terrific pain, and went into collapse. Symptoms of a left sided empyema rapidly developed, and death occurred during the next day. Necropsy revealed a small fibrous tumor in the posterior wall of the esophagus, containing some nerve fibers, in the center of which was a cavity filled with purulent material. The wall of the tumor had ruptured, discharging its contents into the pleural cavity.

SMITH, Ogden, Utah.

LYMPHATIC CYSTS OF THE NECK. ELDRED B. WAFFLE and FRANK E. FOWLER, Northwest Med. **25**:142 (March) 1926.

Waffle and Fowler report a case of lymphatic cyst of the neck in a girl, aged 5. The swelling was located anterior to the left sternomastoid, was not painful and increased in size when the child cried. It was not freely movable and had no demonstrable connection with the nasopharynx. The cyst was dissected out and had not recurred nine months later. The cysts are believed to arise from budding lymph vessels which have a secretory type of endothelium but which have become closed off.

SCOTT, Philadelphia.

TUMORS OF THE URACHUS: A REPORT OF SEVEN CASES. F. W. RANKIN and B. PARKER, Surg., Gynec. & Obst. **42**:19, 1926.

The urachus may remain patent and not cause any trouble until some disturbance in the bladder or an obstruction to the bladder outlet develops. It may harbor a low grade infection and be the cause of purulent cystitis. The author reports such a case and also one of a cyst and one of an abscess of the urachus. Solid tumors occur, and a case each of a fibroma, an adenoma extending into the bladder, an epithelioma and an inoperable adenocarcinoma are described. One case, clinically tuberculosis of the urachus but not proved so, is also presented.

A CONGENITAL CYSTIC TUMOR OF THE NEURENTERIC CANAL. G. H. HAUSMANN, Surg., Gynec. & Obst. **42**:24 (Jan.) 1926.

In an infant, 1 day old, there was found resting on the anterior surface of the sacrum a cystic tumor, which was attached by a pedicle to the anterior surface of the cord through a defect in the sacrum. Histologically, the pedicle had a small lumen lined by epithelial cells, and the wall was made up of glia fibrils and cells. The cyst wall had a stratified squamous epithelial lining, and embedded in the tumor were a few small strands of cartilage, smooth muscle and myxomatous fibrous tissue, nerves and blood vessels.

N. ENZER.

Miscellaneous

ULTRAVIOLET THERAPY IN PEDIATRICS. EDWIN T. WYMAN, Boston M. & S. J. **194**:202 (Feb. 4) 1926.

Mild cases of rickets are treated with cod liver oil alone, but severe forms also receive ultraviolet irradiations. The length of time required to cure severe cases, as shown by roentgenogram and the serum calcium and phosphorus concentration, is from six to eight weeks. When the children are discharged from the "light clinic," cod liver oil is continued to prevent the recurrence of the disease. For tetany, the treatment followed in this clinic is to give from 10 to 20 grains of calcium chloride three times a day, in addition to ultraviolet irradiation. The results have been uniformly good. If rickets is present, as is often the rule, the treatments are continued until the rachitic processes are healed. After the patients are discharged from the "light clinic," cod liver oil is continued to prevent the recurrence of rickets, and the calcium chloride is continued for a time to prevent the recurrence of tetany.

Good results have also been obtained in a few patients with tuberculosis of the mediastinal and mesenteric glands (tuberculous peritonitis), and in a few cases of bronchial asthma in which the child had a sensitization to bacteria. The author has found it impossible to give premature infants sufficient cod liver oil to prevent the occurrence of craniotabes, and suggests: "If it can be determined that ultraviolet therapy will prevent caniotabes and the occurrence of rickets in these infants, it would be a simple procedure to install such lights in premature wards."

Reference is made to beneficial results reported by other observers in skin diseases, erysipelas, ringworm, malnutrition, chronic bronchopneumonia and chronically infected tonsils, etc.

A Room for Treatment with Ultraviolet Rays. Edwin T. Wyman, Boston M. & S. J. **194**:205 (Feb. 4) 1926.

This room was installed at the Infants Hospital, Boston, in order to increase the use of ultraviolet therapy by having a room in which a number of patients could be treated at the same time. Illustrations of the room are given, and also the following description of its installation and manner of technic:

"The light room is 12 feet 6 inches long, 10 feet 10 inches wide and 12 feet high, in which are installed four Burdick, air cooled, mercury vapor quartz lamps, equipped with automatic starting controls. The lamps are placed near the ceiling (a lamp in each corner of the room), 3 feet from the end and 2 feet 9 inches from the side of the room. They are attached to two 2 by 4 inch stringers, which are supported by two 2½ inch pipes, which run the length of the room. The vertical distance from the burners to the floor is 10 feet, and the vertical tube distance (from the patient to the burner) is 7 feet 6 inches. The rheostats controlling the burners are enclosed in a cabinet at one side of the room, and individual rheostats are used for each burner.

"The ventilation of the room is attained by a 12 inch fan in the top of the window on the side of the room, and a register near the floor at the opposite side of the room. A radiator is placed in front of the register to warm the incoming air. The speed of the fan is regulated by a rheostat on the control cabinet. With this arrangement, except in very hot weather in summer, the temperature of the room can be controlled and the gases from the burners eliminated to a large degree. In warm weather, the door on the side of the room opposite the fan is opened to allow better ventilation.

"The entire surface of the baby with the exception of the head, is exposed. This is protected by a sheet draped loosely over the head of the crib and coming down around the baby's neck. The front and back are given the same exposure.

"The following exposure schedule is used in the room: The patients are divided, because of the variation in skin tolerance, according to their complexions —light, medium, dark and black. The light complexioned patients are started at two minutes exposure, front and back, and the time of exposure increased two minutes, front and back, until a total exposure of thirty minutes, front and back is given. The medium complexioned patients are started at three minutes, front and back, and increased three minutes front and back, each exposure, until a total of forty minutes, front and back is given. The dark complexioned patients are started at four minutes, front and back, until a total of fifty minutes, front and back, is used. The black or negro babies are started at five minutes, front and back, until a total of sixty minutes, front and back is given. The treatments are given once a day. We have found that to get the desired results, the black or negro baby has to have twice the exposure of the light complexioned baby."

Conclusions.—A room with a number of mercury vapor quartz lamps suspended just below the ceiling is a practical and efficient way of giving ultraviolet irradiations to a number of patients at the same time. The use of such room has the further advantage in requiring fewer nurses than when individual lamps are used, thereby resulting in a saving of time, which is important from the administrative point of view; the possibility of producing unnecessary erythema is reduced by using a long tube distance, and the life of the burners is materially increased because of their fixed position and the freedom from jars or shocks incidental to moving the lamp to different parts of the hospital. The automatic starting control eliminates the necessity for manually producing the

mercury arc in the burner. Should ultraviolet irradiations prove to be useful as a prophylactic measure against "acute upper respiratory infections" in children, such rooms may find a place in kindergartens and schools, in which the children can have irradiations daily during their rest hours.

GENGENBACH, Denver.

LITTLE MOTHER'S LEAGUES. H. E. KLEINSCHMIDT, J. Social Hyg. **12**:129 (March) 1926.

These organizations are made up of girls from 10 to 16 years old, self-managed, under the direction of a physician or nurse. They offer a means of giving instruction in home-making and infant hygiene. The writer urges that, in addition, they be taught the knowledge essential for intelligent motherhood. Through the dissemination of their training, he feels that much of the mortality associated with child-bearing may be prevented.

GIFTS OF SPRING. MILDRED E. REEVE, J. Social Hyg. **12**:137 (March) 1926.

This article describes the methods employed in the Hathaway-Brown school to teach the small children the principles of life, through the observation of small animals brought to the school and kept for observation.

TRAINING FOR PARENTHOOD. FLORENCE H. RICHARDS, J. Social Hyg. **12**:144 (March) 1926.

Constructive training for the problems of life should begin during infancy and continue throughout life. By permitting the child to learn the facts of life in a simple, natural manner, and to develop rational habits of self-control and daily hygiene, the proper attitude is obtained. This knowledge is supplemented by proper courses in the classroom.

A SOCIAL AND RELIGIOUS VIEW OF THE HOME. ALFRED NEWBERRY, J. Social Hyg. **12**:149 (March) 1926.

The home is the rational place for the child to obtain his training for meeting social problems. This is only possible when the home life is in accord with social principles. Familial disharmony leads to many cases of juvenile delinquency. Lack of harmony and cooperation in the home may be as pernicious in this respect as divorce. The rapid increase in divorce rate is credited to the increasing freedom of women. Sex antagonism is the chief inciting cause. The social sanction of divorce has changed the attitude toward marriage, and greatly lowered the bonds which serve to hold the family intact.

BOYD, Iowa City.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

Jan. 19, 1926

GEORGE E. BAXTER, M.D., *in the Chair*

BOW-LEG AND KNOCK-KNEE. Presented by DR. EDWIN W. RYERSON (by invitation).

The rachitic deformities are not so common as formerly because of better sanitation, increased knowledge on the part of the people as a whole and physicians in particular, but some still remain. Bow-leg is almost always due to rickets, but some children are born with the legs definitely bowed. The congenital type as a rule needs no treatment, but the rachitic types do not always improve spontaneously. It is important to correct bow-leg in the early stages, because if allowed to continue the condition may cause peculiar mental obsessions in later life. It is not difficult to cure in children under 3 years by means of a simple iron brace fastened on the innerside of the leg, with pads at the knee and ankle. This should straighten the legs in eight months or a year. In addition to the braces, it is well to give cod liver oil, phosphorus and calcium. In older children operation is necessary, simply a greenstick fracture which can be produced by the osteoclast and put in casts. The dangers are not great, but a very few patients may develop fat embolism or acidosis. The young adults and older patients require osteotomy.

Knock-knee is not so common as bow-leg but is more disfiguring. The braces used for correction extend from the foot to the hip, and should have no joint at the knee. This condition requires about the same length of time for cure as of bow-leg. Both of these deformities can almost always be cured without difficulty if detected early enough, so that no operating has to be done in the vast majority of cases.

The rachitic spine causes a kyphosis that is long and rounded, and muscular rigidity (spasm) is often present. It is not a sharp, angular kyphosis, because this does not occur unless some severe disease is present, such as tuberculosis, syphilis or cancer. It should be treated with plain Taylor braces, and no casts should be used because plaster casts cause bone atrophy.

The hollow chest of rickets *(pectus excavatum)* is incurable and lasts through life.

Most of the cases of cerebral spastic paralysis, quadriplegia, etc., can be traced to intracranial hemorrhage or other birth injury, and it is important to recognize such conditions at birth, for hemorrhages can be relieved very shortly after birth by proper operative procedure. Obstetricians frequently overlook the milder degrees of hemorrhage, and inestimably valuable time is often wasted. Lumbar puncture should be made in every questionable case.

DISCUSSION

DR. GEORGE E. BAXTER: How long would you think it wise to let bow-leg go without some mechanical interference?

DR. RYERSON: Not over two and a half years at most.

DR. JOSEPH BRENNEMANN: Do you feel that bow-leg is as definitely due to rachitic manifestations as knock-knee? I have felt that the etiologic factors are not exactly parallel between the two. I was surprised to hear Dr. Ryerson speak of using braces in the cases of bow-leg, for I have never seen a subject in whom I though braces were indicated. In fact, I thought they were no longer being used.

DR. RYERSON: I have seen several cases of knock-knee that I felt came definitely from the position in which the child sat on the floor, and have seen in others the condition due to arthritis and fractures. I believe there might be other causes than rickets, but I do not know what they are. I know of no reason why children should develop these conditions without having rickets, and yet I know of dozens of patients in whom no one could find definite signs of rickets. I recall one case in which a child had bow-leg and after recovering from that deformity developed knock-knee, which was cured by operation. Later, the legs became bowed again. Bone atrophy occurs at all ages, but usually has some definite cause. Flatfoot and bow-leg usually go together and knock-knee and varus, and in treating one deformity the other can be corrected. A child with bow-leg should not be permitted to do much walking without braces. They do not mind the braces, and if properly handled can be made to believe it is a distinction to wear them. I think they are quite beneficial.

FLATFOOT IN INFANTS AND IN CHILDREN. Presented by DR. PHILIP LEWIN (by invitation). (Published in full in AMERICAN JOURNAL OF DISEASES OF CHILDREN, May Issue.)

DISCUSSION

DR. JOSEPH BRENNEMANN: I am very frequently asked what kind of shoes a child should wear, whether low or high, soft soled or hard soled, and would like to have Dr. Lewin's opinion on that. I would also like to know what degree of pigeon-toe should be treated.

QUESTION: Dr. Lewin spoke of children never being permitted to go barefooted or to wear gymnasium shoes, and I would like to know if the healthy child should be debarred from this.

DR. LEWIN: So far as gymnasium shoes are concerned, I think they are contraindicated unless the child is doing gymnasium work. A healthy child will break down his longitudinal arch if he is allowed to walk to and from school in such shoes over the hard pavements.

I believe children should wear high shoes, and believe the laced variety is better than the buttoned. I think these should be worn from the time the child begins to walk. We must face the situation that these children are walking on hard floors and pavements, and should have some support. The modification of the heel depends on the size of the child's foot. A tilted heel helps to raise the arch of the foot and the child should come down on the heel first.

A moderate amount of pigeon-toe is a good thing. If it is pronounced enough to need treatment, I think the simplest method is to raise the outer border of the sole. I think many cases of strain of the longitudinal arch are caused by having the outer border of the sole tilted and nothing else done. This should be counteracted by putting a felt pad under the scaphoid and cuneiform, i. e., under the longitudinal arch.

The frequency of flatfoot in infancy is difficult to estimate, and cannot be determined by inspection. I believe every child has a definite arch, but this often is filled with a pad of fat so that it looks flat.

ST. LOUIS PEDIATRIC SOCIETY

Jan. 29, 1926

ADRIEN BLEYER, M.D., *President, in the Chair*

FETAL MONSTROSITIES: THEIR RELATION TO DYSTOCIA. Presented by DR. E. LEE DORSETT (by invitation). This paper was illustrated by lantern slides.

SOME ANATOMICAL PROBLEMS IN PEDIATRICS. Presented by DR. H. A. HARRIS, University College, London (by invitation).

Roentgenograms of embryos, from 52 to 90 days old, were discussed from the point of view of ossification in the skull, spinal column, limb girdle and limbs. A series of roentgenograms of stillborn babes was used to demonstrate the high incidence of cervical rib, premature ossification of the cricoid, and the wide degree of variation in the time of appearance of various centers of ossification. The importance of the diarthrodial joints between the lateral masses of the cervical vertebrae was stressed, as disease in the cervical region differs markedly from disease in any other part of the spinal column.

The development of the skull was discussed, and roentgenograms were used to show the gradual evolution and decay of the diploe and its venous sinuses. The relation of age to the clinical manifestations of fracture of the skull was discussed, and the atypical clinical features and atypical spread of middle ear disease in the first year of life was analyzed in terms of the individuality of the component parts of the temporal bone.

The early appearance of enamel formation in the temporary teeth during the fifth month of fetal life, and the formation of enamel in the first permanent molars before birth was used as a plea for antenatal dietetic care of the mother. The relation of carious molars to the tonsils was stressed, and a plea was made for more active treatment of the teeth and more conservative treatment of the cranial air sinuses.

Roentgenograms and histologic section of rickets, craniotabes and fetal dysostosis cleidocranialis were shown, and the value of roentgenographic diagnosis in rickets was compared with the inconstancy of such signs as a palpable rachitic rosary, sweating and craniotabes.

DISCUSSION

DR. EDWIN P. LEHMAN, in commenting on Dr. Harris' paper, presented a number of bony malformations, discussing them from the surgical point of view.

DR. ERNEST SACHS discussed spina bifida and its development.

DRS. ARTHUR W. PROETZ and ARTHUR M. ALDEN discussed the relation of the development of the structures of the ear, nose and throat, to infection in early childhood.

Book Reviews

DISEASE PREVENTION. By HERBERT H. WHITE, M.D. Price, $4.50. Pp. 680. New York: Thomas V. Crowell Company, 1926.

Although the author of this volume modestly disclaims any attempt to have written an exhaustive treatise on the prevention of disease, this "digest" covers 700 well filled pages. The greater part of the book is a discussion of infectious diseases classified mainly according to methods of transmission. This seems a logical procedure to follow, although certain difficulties are encountered, with the result that material on some diseases is necessarily divided since more than one mode of spread may be involved. For example, typhoid fever comes under "Diseases Spread Through Intestinal Discharges," under water borne diseases, and under milk borne infections. Plague is discussed as a disease transmitted from animals to man and also as an insect borne disease. Hookworm might have been classed as a soil borne disease as well as an infestation, spread by intestinal discharges. Unless the reader is familiar with such diseases, valuable material could readily be missed. It must be acknowledged that the author has been successful to a large extent in avoiding repetition of material.

Each disease is described as to its history, incidence, susceptibility of the human host, cause, source of infection, modes of transmission, immunity toward it and methods of prevention. If any infectious disease is omitted, the reviewer is unaware of it and many diseases are included which are not ordinarily described in books on preventive medicine.

Certain general discussions are also included. The historic introduction is perhaps unnecessarily long, and the chapter on epidemiology disappointing because of its brevity. No discussion of vital statistics is included, although this subject is fundamental to all public health work.

In a book intended for general rather than medical readers, the reviewer appreciates the necessity of the use of simple language, which in many circumstances results in somewhat wordy statements. However, too general statements sometimes leave wrong impressions. The prevention of botulism is not so simple as is indicated because it seems impossible to persuade housewives to boil canned goods, and certainly olives or canned meats served cold would never be heated. The author might just as well have given the latest available typhoid fever death statistics as to have hazarded a guess concerning the number of typhoid deaths in 1925. In 1924, in the registration area, there were about twenty-five diseases with death rates higher than typhoid fever. "Ninth or tenth place" is quite incorrect. The speculative statement concerning the effect of antityphoid vaccination on the number of typhoid carriers might have been omitted. The subcutaneous tuberculin test is not in wide use for clinical diagnosis of human beings. While it is possible to prevent meat borne paratyphoid infections by cooking, the temperatures ordinarily attained in cooking meats are not high enough to destroy these organisms. In the light of our present knowledge, the statements concerning botulism might have been made in less cautious language.

While the foregoing are examples of loose statements, it would be quite unfair to give the impression that the book as a whole is unreliable. Quite the reverse is true. This is almost a monumental work, and teachers and

students will be glad to find so much valuable material gathered in one volume and presented in so readable a manner.

Little attention is given to industrial hygiene, although the principles of prevention are discussed. The infant welfare problem is treated in three pages.

PEDIATRIC NOTES. By WILBURT C. DAVISON. Second Edition. Cloth. Price, $1.25. Pp. 76. Baltimore: Waverly Press, 1926.

In Dr. Davison's excellent little book of seventy-six pages, he covers in a concise form the questions which so often come to the mind of the medical student. The sections which are particularly valuable are those which give the normal dosage of drugs for children and the normal standards of development, as well as the normal blood chemistry. It is a very valuable reference book for the student to have with him at the bedside.

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